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CALCIUM AND PHOSPHORUS IN THE SERUM IN RELATION TO RICKETS*

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At the meeting of the American Pediatric Society held in June, 1920, one of us, in discussing a paper by Park and Howland [1] on the effect of cod liver oil on rachitic bones as demonstrated by the roentgenogram, reported that we had found the concentration of the inorganic phosphorus of the serum to be low in rickets. The amount was definitely increased following the administration of cod liver oil. The present communication represents the work on which these statements were based.

Rickets is a disease characterized by a deficient deposition of calcium salts in the bones themselves and in the intercellular cartilage of the epiphyses. Various views have been expressed and various theories advanced to explain the failure of deposition. We have approached the question from the standpoint of the inorganic chemical composition of the blood serum. Inasmuch as the salts of the bones consist preponderantly of calcium phosphate, it would appear likely that the concentration of calcium and phosphorus in the circulating medium must play an important part in the determination of precipitation. We have, therefore, determined the concentration of these elements in the serum of patients with rickets.

Two questions immediately arise in considering the inorganic constituents of the serum, the first is the total concentration of the substances, and the second is the forms in which they are present. We will discuss at the present time only the concentration of these substances.

Calcium.—Determinations of calcium in the blood and serum have been made for fifty years. A summary of the results is given in Table 1.

It will be seen from the figures that the results obtained by different observers, even from animals of the same species, have by no means

* Received for publication June 3, 1921.

* From the Harriet Lane Home, Johns Hopkins Hospital, and the Department of Pediatrics, Johns Hopkins University.

1. Park and Howland: Arch. Pediat. **37**:411, 1920.

been uniform. It must be remembered, however, that many different methods have been used, some of which, in the light of our present knowledge, cannot be considered free from objectionable features. A critical discussion of the causes of variation in calcium determinations on small quantities of material will be discussed in a subsequent paper. Our own experience, based on two thousand or more determinations, leads to the following conclusions: The calcium content of the serum in health is singularly constant. In only two conditions previously studied (tetany and nephritis) is there a striking diminution in the calcium. The calcium content of the serum of normal children is slightly higher than that of adults. It is usually between 10 and 11 mg. per 100 c.c., whereas with adults it is usually from 9 to 10.5 mg. per 100 c.c. There is no appreciable difference between the calcium content of serum and that of plasma. There is regularly no demonstrable amount of calcium in the red blood cells.[2] For this reason we have confined our determinations of calcium to the serum.

Our results with the serum of normal children and adults and with that of normal animals are summarized in Table 2.

Phosphorus.—We are aware of the various fractions into which the total phosphorus of serum may be divided, viz., acid soluble and the acid insoluble. The former includes the inorganic phosphorus and the "rest" or "undetermined phosphorus," while the latter includes the protein and lipoid phosphorus. Little is known at present regarding the equilibrium existing between the various forms of phosphorus in the serum and in the red blood cells or the ease with which an exchange of these substances may take place between the corpuscles

2. We appreciate that calcium has been determined in the corpuscles by different observers (Cowie and Calhoun,[3] Hamburger,[4] Rona and Takahashi,[5] etc.). On the other hand, Abderhalden,[6] who has made the most elaborate study of this particular point, never found any calcium in the corpuscles nor did Bunge[7] before him. In the study of the blood of twenty-six cats, Heubner and Rona[8] found demonstrable amounts of calcium in only six. Falta and Richter-Quittner[9] regularly failed to find any calcium in a large number of determinations. Howland and Marriott[10] were not able to demonstrate the presence of calcium in human corpuscles. In a study of the blood of seven normal adults, Tisdall and Kramer, in this laboratory, failed to find more than 1 mg. calcium in 100 c.c. of corpuscles. This is well within the limits of error of any micromethod. In another place we will discuss the possible sources of error in such determinations.

3. Cowie and Calhoun: J. Biol. Chem. **37**:505, 1919.
4. Hamburger: Ztschr. f. physik. Chem. **69**:663, 1909.
5. Rona and Takahashi: Biochem. Ztschr. **31**:336, 1911.
6. Abderhalden: Ztschr. f. physiol. Chem. **34**:65, 1898.
7. Bunge: Ztschr. f. Biol. **12**:191, 1876.
8. Heubner and Rona: Biochem. Ztschr. **93**:187, 1919.
9. Falta and Richter-Quittner: Wien. Arch. **2**:1920.
10. Howland and Marriott: J. Biol. Chem. **32**:233, 1917.

and plasma. Therefore, precautions are necessary in the determination of phosphorus. We have controlled certain factors which bear directly on our own work. First, as to the changes in the serum itself after separation from the clot. If kept on ice even for several days, there is

TABLE 1.—CONCENTRATION OF THE CALCIUM IN SERUM OR PLASMA

Author	Year	Source	Calcium, Mg. per 100 C.c. Serum
E. Abderhalden	1898	Pig	8.7
E. Abderhalden	1898	Ox	7.9
E. Abderhalden	1898	Sheep	8.4
E. Abderhalden	1898	Goat	8.6
E. Abderhalden	1898	Dog	8.1
E. Abderhalden	1898	Horse	7.9
E. Abderhalden	1898	Rabbit	8.3
E. Abderhalden	1898	Cat	7.8
G. Bunge	1876	Pig	9.7
G. Bunge	1876	Cow	9.0
R. Pribram	1871	Horse	12.8 (aver.)
L. Gerlach	1872	Dog	10.0
P. Rona and D. Takahashi	1911	Cow	9.2
P. Rona and D. Takahashi	1911	Pig	9.6 (aver.)
P. Rona and D. Takahashi	1911	Horse	12.3 (aver.)
W. Heubner and P. Rona	1919	Cat	11.4
H. Stheeman	1921	Infant	8.6-9.3
Howland and Marriott	1918	Infants	10-11
Howland and Marriott	Unpublished	Cow	10.3
Halverson and Bergeim	1917	Ox	10.3
Halverson and Bergeim	1917	Human	10.0
Halverson and Bergeim	1917	Human	10.0 (aver.)
G. W. Clark	1920	Rabbit	12.6 (aver.)
Meigs, Blatherwick and Cary	1919	Heifer	9.7 (aver.)
Meigs, Blatherwick and Cary	1919	Heifer	9.7 (aver.)
Denis and Talbot	1921	Normal adults	7.2-12.1 (aver. 10)
von Meysenbug	1921	Normal infants	11.2 (aver.)

little, if any, change. We have found a slight increase or a slight diminution, but usually the results are the same. This is true not only of serum from normal adults but from normal children and rachitic children. We have not allowed the serum to stand at room temperature, except during the precipitation of the phosphate, but we have found no essential change when samples have been filtered after forty-eight or seventy-two hours at room temperature. On the other hand, when

TABLE 2.—RESULTS OF CALCIUM DETERMINATIONS MADE BY AUTHORS

Subject	Number of Determinations	Minimum	Maximum	Average
Nonrachitic children under 2 years	13	10.2	11.0	10.7
Placental blood	7	10.4	11.3	10.8
Adults	20	9.3	10.6	10.0
Dog	7	10.8	11.6	11.2
Sheep	6	10.1	10.5	10.3
Rats	8	9.2	10.1	9.6

serum is allowed to stand in contact with the clot at room temperature, a rapid increase of the orthophosphate occurs. Thus in one instance an increase from 2.0 to 12.5 mg. of inorganic phosphorus in 100 c.c. of serum was noticed after forty-eight hours, and in another case an

increase from 2.6 to 11.0 mg. was found in the same length of time. When kept on ice, serum may occasionally be in contact with the clot without serious change in the orthophosphate content, even for several days, but it is unwise to allow this, and we have usually precipitated the phosphate as soon as the serum could be freed from the clot.

TABLE 3.—PHOSPHORUS DETERMINATIONS BY VARIOUS AUTHORS

Author	Subject	Inorganic Phosphorus	Acid Soluble Phosphorus	Source
Abderhalden, 1898	Pig	2.3	.....	Serum
	Ox	2.7	.....	Serum
	Sheep	3.2	.....	Serum
	Goat	3.1	.....	Serum
	Dog	3.5	.....	Serum
	Horse	3.3	.....	Serum
	Rabbit	2.8	.....	Serum
	Cat	3.1	.....	Serum
Pribram, 1871	Dog	3.7	.....	Serum
Gerlach, 1872	?	4.8	.....	Serum
Feigl, 1919-1920	Man	...	2.0-4.0	Plasma
	Man	1.0-5.1	1.2-5.7	Plasma
Bloor, 1918	Man	1.9-3.3	2.4-4.4	Plasma
Marriott and Howland, 1918	Man	1.0-3.5	.....	Serum
	35 subjects			
Iverson, 1920	Rabbit	.....	2.2 (aver.)	Serum
	Rabbit	.....	2.8	Plasma
	Guinea-pig	.....	5.1	Serum
	Pigeon	.....	1.7-4.8	Serum
	Rat	.....	5.2	Serum
	Cat	.....	2.4-10.3	Serum
	Dog	.....	2.0-4.0	Serum
	Cow	.....	4.1	
Meigs, Blatherwick and Cary, 1919	Cow	4.5		
Greenwald, 1915	Human	.....	3.6	Serum

TABLE 4.—INORGANIC PHOSPHORUS DETERMINATIONS BY AUTHORS WITH SERA OF NONRACHITIC CHILDREN AND NORMAL ADULTS

Subject	Age	Inorganic Phosphorus, Mg. per 100 C.c. Serum	Subject	Inorganic Phosphorus, Mg. per 100 C.c. Serum
Nonrachitic child	4 months	6.8	Adult	1.8
Nonrachitic child	7 months	5.3	Adult	2.8
Nonrachitic child	2 years	4.9	Adult	2.0
Nonrachitic child	3 months	6.5	Adult	1.8
Nonrachitic child	8 months	5.4	Adult	1.9
Nonrachitic child	11 months	5.3	Adult	1.6
Nonrachitic child	18 months	5.0	Adult	2.5
Nonrachitic child	9 months	5.0	Adult	2.9
Nonrachitic child	16 months	6.0		
Nonrachitic child	10 months	4.5		
Nonrachitic child	22 months	5.0		
Nonrachitic child	22 months	4.8		
Average	.....	5.4	.....	2.1

We have concerned ourselves only with the determination of the inorganic phosphorus of the serum. This represents the orthophosphate content of the serum, the only form of phosphate which can react with calcium to form tertiary calcium phosphate. There can be no doubt that the inorganic phosphorus represents a definite chemical entity, since it is present in nearly constant amount in the same individual as well as in normal individuals of the same age. This

amount is essentially the same whether determined upon plasma or serum. The determination is made with a minimum of chemical manipulation and there is therefore slight chance of transforming one form of phosphorus into another.

In Table 3 are included the determinations of the phosphorus of the serum of different animals by different authors. In some cases the inorganic phosphorus was determined, in others the so-called acid soluble fraction.

In Table 4 we present some of the determinations of inorganic phosphorus made by ourselves on the serum of nonrachitic children 2 years of age and less, and on that of normal adults.

This table shows that the figures for each of these two age groups are fairly uniform, but that the two groups differ in that the serum of adults regularly contains much less inorganic phosphorus than that of infants.

It has been demonstrated that in tetany there is regularly a very great reduction in the calcium of the serum. Howland and Marriott [11] had previously reported a number of determinations of calcium made on the serum of rachitic patients, and came to the conclusion that while there was a moderate reduction of the calcium in the majority of cases, there was a normal calcium content in at least one-third of the cases of active rickets. They suggested that the reduction of the calcium in rickets might indicate a latent tetany, and this view was supported by the almost constant occurrence of anodal hyperexcitability in those patients in whom the calcium of the serum was somewhat reduced. Aschenheim [12] made a number of determinations of the calcium of the blood of rachitic children obtained by cardiac puncture postmortem. He found marked variations, from 2.6 to 12.7 mg., of calcium per 100 c.c. of blood. In view of the well known fact that the corpuscles contain practically no calcium, these determinations have little weight as the relative proportion of corpuscles and serum was not determined.

We determined the calcium of the serum in a large series of cases of rickets. It soon became evident that there are other factors to be considered since the inorganic matter of bone consists, in the main, of calcium phosphate with a much smaller amount of calcium carbonate. It seemed clear, therefore, that other substances should be determined, that is, the bicarbonate and the orthophosphate of serum or plasma. As calcium phosphate forms from 85 to 90 per cent. of the salts of bone, and is by far the least soluble salt, it seemed sufficient to confine ourselves to a study of the concentration of calcium and the orthophosphate of the serum.

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11. Howland and Marriott: Quart. J. M. **11**:289, 1918.
12. Aschenheim: Jahrb. f. Kinderh. **79**:446, 1914.

Our studies have been made on children with rickets between the ages of 3 months and 3 years. The diagnosis of rickets has been made in every instance on clinical grounds supported by roentgenograms. The significance of the latter in the diagnosis of rickets will be discussed elsewhere in detail. Suffice it to say at the present time that we have used only those children who have shown unmistakable evidences of the disease, such as irregularity of the ends of the long bones, a fringed appearance, or cupping of the extremities of the diaphyses and an absence of normal centers of ossification in the epiphyses. Associated with these changes were rarefaction of varying degrees of severity and not infrequently fractures of the shafts of the bones or dislocation of the epiphyses. Roentgenograms were made periodically of those patients who were treated by cod liver oil. Evidences of healing, i.e., of the deposition of calcium salts, were shown after a time by a shadow in that portion of the metaphysis (transitional zone) which was previously translucent to the roentgen ray. This usually took the form of a line on the epiphyseal side of the metaphysis; by the appearance of centers of ossification or, if these had been present but indistinct, by a sharpening of their shadow and after the lapse of a period of weeks by an increase in the density of the bones. In the cases of a few patients who died subsequently of some other disease, an opportunity was given to confirm the diagnosis of rickets by macroscopic and microscopic examination of the bones.

We have made our studies during all the months of the year, but the great majority of determinations were made in the winter and spring months. It is well known, from clinical observation, and from the pathologic studies of Schmorl[13] that rickets is a disease much more prevalent and severe in the winter and spring. It undoubtedly undergoes spontaneous cure in many instances in the summer and autumn months. The fact that our studies were made on young children, most of whom were under 2 years of age, and chiefly in the winter and spring months, eliminates, so far as is possible, the influence of spontaneous cure.

When a diagnosis of rickets was made, it has been our practice to obtain a specimen of serum and to make determinations of the calcium and phosphorus at once. The methods used have been described elsewhere.[14] Treatment with cod liver oil was then instituted, the amount varying somewhat with the weight of the child, but generally from 2 to 4 c.c. were given, three times a day. Treatment was uninterruptedly

13. Schmorl: Ergebn. d. inn. Med. u. Kinderh. **4**:403, 1909.

14. Marriott, Howland and Haessler: J. Biol. Chem. **32**:233, 1917; Kramer and Howland: J. Biol. Chem. **43**:35, 1920; Kramer and Tisdall: Johns Hopkins Hosp. Bull. **32**:44, 1921.

continued when patients were in the hospital.[15] Thereafter determinations were made at different intervals of time, a roentgenogram also being taken. It has thus been possible to correlate the chemical with the anatomic changes.

For purposes of comparison with rachitic patients, we insert Table 5 to show the inorganic phosphorus content of the serum of sixteen nonrachitic children. Duplicate determinations were made with all; with some several determinations were made. The average was 5.4 mg. per 100 c.c. Six children were partly or wholly breast fed. The average for these was 6.1 mg. per 100 c.c. Sixteen children were fed on milk or soft diet in which milk played a large part. The average for these was 5.1 mg. It appears that breast fed children have a

TABLE 5.—THE PHOSPHORUS CONTENT OF THE SERUM OF NONRACHITIC CHILDREN *

Name	Age	Date	Diet	Phosphorus
E. C.	7 mos.	10/ 8/20	Protein milk	5.4
M. H.	2 yrs.	10/ 8/20	Soft diet	4.7
		10/ 9/20	Soft diet	5.2
W. M.	3 mos.	10/ 8/20	Protein milk and breast milk	6.0
		10/ 9/20	Protein milk and breast milk	7.1
A. K.	8 mos.	10/ 8/20	Protein milk	5.6
		10/ 9/20	Protein milk	4.8
E. D.	11 mos.	10/ 8/20	Protein milk and junket	5.6
		10/ 9/20	Protein milk and junket	5.4
H. T.	6 wks.	10/ 9/20	Protein milk	5.0
E. G.	9 mos.	10/ 9/20	Protein milk	5.4
		10/ 9/20	Protein milk	5.4
R. M.	16 mos.	10/10/20	Soft diet	5.0
		10/10/20	Soft diet	4.8
H. V.	10 mos.	10/10/20	Protein milk	4.5
		10/10/20	Protein milk	4.0
F. H.	4 mos.	8/10/20	Breast fed	6.8
D. M.	2 mos.	3/22/21	Breast fed	5.6
R. J.	4¾ yrs.	3/ 1/21	Soft diet	5.3
B. S.	19 mos.	3/ 1/21	Breast and soft diet	5.0
M.	5 yrs.	2/ 3/21	General diet	5.0
I. Z.	2 yrs	1/23/21	General diet	4.8
B.	4 mos.	6/14/20	Breast fed	6.0

* Roentgenograms of the bones of these children showed them to be normal.

somewhat higher inorganic phosphorus content of the serum than the artificially fed. Age during the first two or three years does not seem to affect the inorganic phosphorus in the serum, except in so far as breast feeding plays a part with those less than 1 year of age. The absence of rickets in all these children was determined by clinical examination and by roentgenograms.

We have determined the concentration of inorganic phosphorus and calcium in the serum of twenty-two rachitic children who had never been treated. The magnesium was also determined in the serum of four of these. The concentration of phosphorus with these patients varied from 0.6 to 3.2 mg. per 100 c.c. The average was 2.0 mg., less than 50 per cent. of the normal serum content.

15. Our experience with patients in the outpatient department has been very unsatisfactory and many observations have had to be discarded because the mothers would not return sufficiently often to make the treatment continuous.

In Table 7 is shown the influence of cod liver oil on the inorganic phosphorus and calcium of the serum. An increase in the phosphorus is readily apparent. The amount of calcium was not strikingly influenced. The increase in the inorganic phosphorus was from an average of 1.9 to an average of 5.5 mg. per 100 c.c. of serum. The earliest chemical changes do not usually occur in less time than two weeks after the administration of cod liver oil. There is a gradual increase, until at the end of from five to six weeks an amount is reached which is about the average for young children or slightly above this. The concentration of phosphorus is maintained at this point indefinitely so long as cod liver oil is given. We have a few observations to show that if medication is stopped, the amount of phosphorus diminishes again.

TABLE 6.—THE CONCENTRATION OF CALCIUM, PHOSPHORUS AND MAGNESIUM IN SERA OF RACHITIC CHILDREN

Name	Age	Date	Calcium, Mg. per 100 C.c. Serum	Phosphorus, Mg. per 100 C.c. Serum	Magnesium, Mg. per 100 C.c. Serum
G. E.	8 mos.	5/13/20	10.1	2.0	2.5
B. J.	18 mos.	10/26/20	9.3	2.0	
M. J.	2½ yrs.	10/14/20	9.8	2.2	
M. J.	2½ yrs.	10/27/20	9.7	2.8	
L. P.	6 mos.	10/27/20	8.0	1.0	2.2
J. M.	3 yrs.	10/22/20	7.5*	1.8	
J. C.	8½ mos.	10/29/20	7.7*	0.6	1.8
M. T.	6 mos.	11/18/20	10.3	2.4	
J. J.	6 mos.	11/18/20	7.8*	3.0	2.3
V. G.	7 mos.	2/ 4/21	...	1.8	
E. B.	1 yr.	3/ 5/21	10.8	2.8	
H. G.	3 mos.	3/ 7/21	...	2.2	
M. C.	17 mos.	3/15/21	...	1.6	
J.	.....	3/10/21	9.8	2.8	
M. H.	1 yr.	3/10/21	9.1	1.9	
E. B.	6 mos.	3/16/21	...	1.5	
H. K.	.....	3/24/21	10.0	1.0	
W. J.	.....	4/ 1/21	9.3	1.4	
J. S.	2 yrs.	4/17/20	8.7	2.0	
B.	.....	4/21/20	10.5	3.2	
M. G.	.....	1/ 5/20	9.0	2.2	
C. S.	10 mos.	4/29/20	...	1.5	
L. S.	10 mos.	4/29/20	...	2.0	

* Latent tetany—anodal reversal.

From an examination of Tables 6 and 7 it may be seen that excluding cases of frank tetany, the calcium content of the serum in twelve out of twenty-five cases fell within normal limits. In the remaining thirteen cases the concentration of calcium was lower than normal, but usually not significantly so, and for reasons that have been mentioned before the possibility of a latent tetany is always to be thought of as influencing the amount of calcium. It seems sufficiently plain that rickets, even in a severe form, may be present, and yet the calcium content of the serum be normal in amount. Calcium deficiency in the serum cannot, therefore, be looked on as the primary reason for failure of calcium deposition.

TABLE 7.—THE CONCENTRATION OF CALCIUM, PHOSPHORUS AND MAGNESIUM IN THE SERUM OF CHILDREN WITH RICKETS BEFORE AND AFTER TREATMENT WITH COD LIVER OIL

Name	Age	Date	Ca	P	Mg	Cod Liver Oil	Remarks
L. B.	5 mos.	12/ 3/20	8.8	2.9	2.8	.....	Roentgenogram showed mild but unmistakable rickets
		2/ 3/21	8.5	6.6	3.2	2 c.c., t. i. d., for 2 mos.	Roentgenogram showed evidences of healing
M. C.	35 mos.	4/30/20	10.5	1.8	...	May 1 and thereafter	Roentgenogram showed very marked rickets evidently of long duration
		5/20/20	10.2	9.0	1.6	4 c.c., t. i. d., for 3 weeks	Distinct evidences of healing by roentgenogram
C. H.	9 mos.	4/13/20	9.8	1.6	...	April 16 and thereafter	Marked rickets by roentgenogram
		5/26/20	11.0	6.8	...	2 c.c., t. i. d., for 6 weeks	Definite evidences of healing
W. P.	27 mos.	10/27/20	9.6	0.8	2.3	.....	Marked rickets by roentgenogram
		11/ 3/20	9.7	1.2			
		1/10/21	10.0	6.0	...	2 c.c., t. i. d., for 10 weeks	Healing complete
E. S.	12 mos.	6/15/20	10.0	3.4	3.7	.....	Roentgenogram showed distinct rickets with fracture
		11/22/20	....	5.0	...	2 c.c., t. i. d., for 5 mos.	Healed rickets
		3/30/21	....	5.0	...	.....	Healed rickets
R. R.	12 mos.	1/19/21	....	3.2	2.2	.....	Roentgenogram showed marked rickets evidently of long standing
		3/10/21	....	4.4	...	4 c.c., t. i. d., for 10 weeks	Roentgenogram showed unmistakable evidences of healing
		4/ 3/21	...	5.6			
A. Y.	36 mos.	5/17/20	10.2	1.6	...	.....	Severe rickets by roentgenogram
		6/25/20	....	3.2	...	4 c.c., t. i. d., for 7 weeks	Evidences of healing
J. S.	24 mos.	4/17/20	8.7	2.0	...	.....	Roentgenogram showed severe rickets
		5/26/20	8.2	3.2	2.3	4 c.c., t. i. d., for 5 weeks	Unmistakable evidences of healing
M. C.	17 mos.	3/15/21	....	1.6	...	.....	Roentgenogram showed very severe rickets
		5/14/21	....	6.6	...	2 c.c., t. i. d., for 2 mos.	Distinct evidences of healing
W. J.	18 mos.	4/ 1/21	9.3	1.5	...	.....	Roentgenogram showed definite evidence of rickets
		4/ 6/21	....	2.8	...	4 c.c., t. i. d., for 42 days	
		5/12/21	....	5.0	...	.....	Distinct evidences of healing
E. W.	36 mos.	4/14/21	....	1.2	...	4 c.c., t. i. d., for 27 days	Roentgenogram showed distinct evidence of rickets
		5/11/21	....	4.6			
A. L.	21 mos.	3/31/21	....	1.0	...	2 c.c., t. i. d., for 3 weeks	Had been receiving cod liver oil for several months, but intermittently on account of diarrhea; the roentgenographic evidences of rickets had disappeared; for some weeks before the first determination of phosphorus he had received no oil, or only 5 drops, t. i. d.; with the increase of cod liver oil the phosphorus rose rapidly
		4/21/21	....	2.8			
		5/11/21	....	4.6			

The findings regarding the phosphorus are, on the other hand, very striking. With all patients in the active stage of rickets (confirmed by roentgenograms) the concentration of inorganic phosphorus in the serum was low. With the healing of the process in the bones that occurred after cod liver oil medication, the phosphorus rose gradually to normal. These facts lead us to consider the presence of a low inorganic phosphorus in the serum of a young child as nearly conclusive evidence of active rickets. Indeed, one of us has occasionally determined the phosphorus without having seen either patient or roentgenogram and has correctly indicated to the other whether rickets was or was not present. *In rickets we believe, therefore, that there is constantly a marked and, for the causation of the pathologic lesion, an important deficiency in inorganic phosphorus. To this deficiency is to be ascribed the failure of calcium deposition.*

The composition of the inorganic constituents of normal bone is difficult to determine, for several reasons, but chiefly on account of the uncertainty of the carbonic acid determination. The most recent determinations by Wells [16] and others and by ourselves show that of the ash from 85 to 90 per cent. is calcium phosphate, from 10 to 15 per cent. is calcium carbonate and a small amount is magnesium phosphate.

In determining the precipitation from the blood and tissue fluids of calcium salts in normal ratio in bone many factors play a part. We must consider the concentration of calcium, phosphorus, bicarbonate, the carbon dioxid tension, the colloids, the reaction (hydrogen ion concentration) and, perhaps, the presence of other salts. The blood serum of infants contains from 10 to 11 mg. calcium per 100 c.c. Pauli and Handowsky [17] showed that electrolytes form compounds with proteins. Rona and Takahashi,[18] by compensation dialysis, demonstrated that from 15 to 25 per cent. of the calcium is nondialyzable, in other words, is probably bound by protein. The remainder is dialyzable. The possible existence of compounds of calcium and protein is made fairly certain by the recent work of Loeb,[19] since proteins at a reaction (p_H) above their iso-electric point (i.e., more alkaline) form compounds with monovalent and divalent cations. But most of the calcium exists in inorganic compounds, and because of its low concentration is practically completely ionized, and, therefore, in a very active form. Moreover, even the calcium presumably in combination with protein, is loosely bound for we have been able to precipitate calcium from serum quantitatively merely by the addition of ammonium oxalate.

16. Wells: Harvey Lecture, 1911, p. 107.
17. Pauli and Handowsky: Beitr. z. chem. Phys. u. Path. **11**:415, 1908.
18. Rona and Takahashi: Biochem. Ztschr. **49**:370, 1913.
19. Loeb: Science **52**:449, 1920.

The inorganic phosphorus concentration in the serum is about 5 mg. per 100 c.c. Rona and Takahashi,[20] in the investigations referred to above, showed that the inorganic phosphorus of serum is wholly dialyzable. This observation is strengthened by the investigations of Loeb [21] who pointed out that gelatine forms no compounds with anions at a p_H above its iso-electric point (more alkaline). The iso-electric point of all the proteins that may be found in serum has not been determined, but such observations as have been made indicate that it is always more acid than the reaction of normal blood. The inorganic phosphates are, therefore, all free in the sense that they are not bound by protein. On account of their concentration they are also probably completely ionized.

The carbon dioxid tension has a profound influence on the form of the calcium salts present and on their solubility. The carbon dioxid tension of normal plasma is from 40 to 45 mm. of mercury. Bohr [22] has shown that at a temperature of 38 C. and at a carbon dioxid tension of 45 mm. of mercury, in a solution containing a concentration of sodium carbonate equivalent to that found in blood, the carbonate is more than 99 per cent. transformed into bicarbonate. The influence of carbon dioxid in transforming the insoluble tricalcium phosphate and calcium carbonate into the relatively soluble acid calcium phosphate and calcium bicarbonate may be indicated by the following reactions:

$$Ca_3(PO_4)_2 + 2H_2CO_3 = 2\ CaHPO_4 + Ca(HCO_3)_2$$

In the presence of carbonic acid, therefore, part of the tricalcium phosphate is transformed into bicarbonate, irrespective of the presence of any other carbonate in the solution. In solutions of calcium phosphate, calcium carbonate and carbonic acid an equilibrium exists between these salts and their component ions. Thus for calcium carbonate ($CaCO_3$) in the presence of carbonic acid (H_2CO_3), the following reaction represents the equilibrium:

$$(1)\ CaCO_3 + H_2CO_3 \rightleftarrows Ca(HCO_3)_2 \rightleftarrows Ca^{++} + HCO_3^{-}$$

In the case of tertiary calcium phosphate the equilibrium is represented by the following reaction:

$$(2)\ Ca_3(PO_4)_2 + 2\ H_2CO_3 \rightleftarrows 2\ CaHPO_4 + Ca(HCO_3)_2 \rightleftarrows 2\ Ca^{++} + 2\ HPO_4^{--} + Ca^{++} + HCO_3$$

From these equations it is obvious that the relative proportion of the different components may be determined by the concentration of free carbonic acid. The concentration of free carbonic acid being fixed, the equilibrium may be disturbed by an alteration in the concentration of any of the other components. Thus in equation (1) the introduction of sodium bicarbonate, which yields a large amount of bicarbonate

20. Rona and Takahashi: Biochem. Ztschr. **49**:370, 1913.
21. Loeb: Science **52**:449, 1920.
22. Bohr: Quoted by Van Slyke, Physiol. Rev. **1**:141, 1921.

ion (HCO_3), would repress the ionization of calcium bicarbonate resulting in the formation of more undissociated calcium bicarbonate than could exist as such at the given concentration of free carbonic acid. The excess would, therefore, be converted into calcium carbonate, and should the concentration of this exceed the solubility of the very insoluble calcium carbonate precipitation would follow. The addition of a calcium salt more soluble than calcium bicarbonate would increase the concentration of calcium ions and a similar sequence of events would follow. Similarly in reaction (2) an increase in the concentration of calcium ion, of phosphorus (HPO_4) ion or of bicarbonate ion, would bring about the ultimate precipitation of tertiary calcium phosphate through the reversal of this reaction. The relative amount of the two salts precipitated would be inversely proportional to their solubility. *On the other hand, a decrease in the phosphorus* (HPO_4) *ion would render more difficult the precipitation of tertiary calcium phosphate.*

In order that these facts may be applied to serum, it still remains to be proven that these calcium salts exist in the blood in a nearly saturated solution. Clinical and pathologic evidence of this is given by the formation of calcium metastases in conditions in which, as the result of bone destruction, it is believed there is a supersaturation of the blood with calcium salts. These calcium deposits are found in those situations where acid is given off, that is in the lungs (CO_2), the gastric mucosa (HCl) and the kidney (HPO_4). Repeated attempts have been made by different investigators [23] to increase the calcium content of the serum by the introduction of calcium salts in various ways. Calcium in the serum may be increased by direct injection into the blood stream or into the tissues but the increase is noticeable for only a few hours. No increase is brought about by feeding calcium salts to animals or man unless there has been a previous reduction in the calcium. In our experience, the feeding of soluble calcium salts to children in large quantities and over prolonged periods does not result in an increase of the serum calcium above the normal.

Studies on the influence of the carbon dioxid tension on the solubility of calcium phosphate ($Ca_3(PO_4)_2$) and calcium carbonate ($CaCO_3$) have been made by several chemists, notably by Seidell,[24] Leather and Sen,[25] Cameron and Seidell,[26] Johnson and Williamson,[27] Kendall [28] and Rona and Takahashi.[29] Their studies demonstrate a

23. Clark: J. Biol. Chem. **43**:89, 1920; Denis and Minot: J. Biol. Chem. **41**:357, 1920; Heubner and Rona: Biochem. Ztschr. **93**:187, 1919.
24. Seidell: Solubilities of Inorganic and Organic Compounds, Ed. 2, D. van Nostrand Co., N. Y.
25. Leather and Sen: Mem. Dept. Agric. Ind. Chem. Serv. **1**:117, 1910.
26. Cameron and Seidell: J. Am. Chem. Soc. **26**:1460, 1904.
27. Johnson and Williamson: J. Am. Chem. Soc. **38**:975, 1916.
28. Kendall: Philosoph. Mag. **23**:958, 1912.
29. Rona and Takahashi: Biochem. Ztschr. **49**:370, 1913.

marked influence of two factors, namely, the carbon dioxid tension and temperature. Thus the solubility of calcium carbonate at 0 mm. carbon dioxid tension and at 15 C. is 6.8 mg. per 100 c.c. This is reduced to 5 mg. when the temperature is increased to 25 C. The solubility of calcium bicarbonate at 38 mm. carbon dioxid tension and at 16 C. is 58 mg. per 100 c.c. This is strikingly increased to 187 mg. at approximately the same temperature, but at a carbon dioxid tension of 68 mm. When the temperature is increased 10 C., in spite of an increase of carbon dioxid tension of 8 mm., the solubility falls to 65 mg. per 100 c.c. It is reasonable to infer, therefore, that at from 40 to 45 mm. carbon dioxid tension and at 38 C. the solubility of calcium bicarbonate would be considerably less than 58 mg. per 100 c.c. If all the 10 mg. of calcium found in normal serum existed as the bicarbonate, there would be 40.5 mg. calcium bicarbonate. It is evident from the figures, therefore, that the serum must be nearly saturated with respect to calcium carbonate ($Ca(HCO_3)_2$).

Measurements of the solubility of the phosphates of calcium in serum have been quite unsatisfactory since in many instances no attention has been paid to the hydrogen ion concentration or to the carbon dioxid tension, two factors greatly influencing the solubility of these salts. *It is a point worthy of note that the ratio of the concentration of calcium to that of phosphorus in the serum of nonrachitic children is practically identical with the ratio of these elements in tertiary calcium phosphate, the salt which composes from 85 to 90 per cent. of the salts of normal bone.* Were all the calcium in the form of tertiary calcium phosphate, the concentration of this salt would be 26 mg. per 100 c.c. The studies of Ehlert and Hempel [30] have demonstrated that even under such favorable conditions as a carbon dioxid tension of two atmospheres and a temperature of 14 C., only 23 mg. calcium phosphate ($Ca_3(PO_4)_2$) are in solution in 100 c.c. of water. With the higher temperature of the body and the lower carbon dioxid tension, the solubility would be greatly reduced. It is apparent, therefore, that under similar conditions serum can maintain a much higher concentration of the phosphates of calcium than can water. Ehlert and Hempel have also shown that the presence of neutral salts has a favorable influence on the solubility of calcium phosphate. But the concentration of salts employed by them was infinitely greater than that which obtains in the blood. Serum contains from 7 to 9 per cent. protein. It is, therefore, reasonable to infer that the colloids exert a profound protective effect against the precipitation of calcium salts quite independently of any effect that they might have by forming chemical compounds with the calcium. Hofmeister [31] states that the colloid influence is very much diminished when the concentration of protein is reduced to 2 per cent.

30. Ehlert and Hempel: Ztschr. f. Electrochem. **18**:727, 1912.
31. Hofmeister: Ergebn. d. Physiol. **10**:431, 1910.

The concentration of protein in lymph varies between 2 and 4 per cent. The amount depends considerably on the tissue from which the lymph is obtained. It is apparent, therefore, that the protective influence which the protein exerts is no longer operative or operative to a much less degree in the tissue fluids. On the other hand, the absolute concentration of calcium bicarbonate and calcium phosphate is essentially the same in the tissue fluids as in serum [32] and the proportion of free calcium must then be actually increased.

As shown by L. J. Henderson [33] and Hasselbalch and Gammeltoft [34] and others, the hydrogen ion concentration (p_H) of the serum depends chiefly on the relation between free carbonic acid and sodium bicarbonate. When the acid is reduced, the serum becomes more alkaline; when it is increased, the serum becomes more acid. The determination of a change in reaction of the fluids in the tissues is obviously a matter of much difficulty, but that the difference in reaction is sufficient to induce precipitation in different parts of the circulatory system is shown by the fact that in the metastatic calcification referred to above the deposition of calcium salts occurs on the arterial side of the capillary system indicating that the slight difference in reaction on the two sides of the capillary system is sufficient to determine precipitation or solution. We may, therefore, visualize the process of calcification as follows: There filters from the arterial capillaries into the intercellular matrix of the cartilage and about the trabeculae a fluid containing calcium and phosphate and bicarbonate in the same concentration as in the serum but with much less protein. A slight reduction in carbon dioxid tension, operative, perhaps, for a short period of time, would result in the precipitation of calcium salts in inverse proportion to their solubility. It seems likely that the reduction of carbon dioxid tension is favored by the extreme metabolic inactivity of bone and cartilage. Liek [35] has shown that the amount of blood supplied to a tissue is an important factor in determining calcification. There is an optimum amount. The freedom of most of the cartilage from calcification may be explained by its very deficient blood supply. Only at a point where the cartilage is in close contact with the circulation from the marrow does calcification of the cartilage occur. The trabeculae of the diaphyses in which precipitation of calcium salts also occurs are likewise in close contact with the marrow. Even if the carbon dioxid tension is restored, the precipitated salts do not redissolve, on account of the well known difficulty of such resolution. On the basis of this

32. Munk and Rosenstein: Virchows Arch. f. path. Anat. **123**:230, 484, 1891.
33. Henderson: Ergebn. d. Physiol. **8**:254, 1909.
34. Hasselbalch and Gammeltoft: Biochem. Ztschr. **78**:112, 1916.
35. Liek: Arch. f. klin. Chir. **85**:118, 1908.

explanation, the failure of calcification to occur in other tissues would depend on their greater metabolic activity and the constant presence of carbon dioxid passing from the cells into the tissue fluids.

In active rickets there is regularly a striking diminution in the phosphate of the serum. The tissue fluids share in the diminution. Conditions are therefore unfavorable for the precipitation of tricalcium phosphate. The difficulty of precipitation would be exaggerated by any reduction of calcium which, as has been shown, occurs in a certain proportion of cases.

CONCLUSIONS

In nonrachitic infants and young children, the concentration of calcium is from 10 to 11 mg. per 100 c.c. of serum.

The concentration of inorganic phosphorus is about 5 mg. per 100 c.c. of serum.

The constancy of the concentration of calcium, phosphorus and bicarbonate in the serum of normal children undoubtedly determines the constancy of the inorganic composition of normal bone.

During the period of active rickets, the calcium concentration may be normal or slightly reduced. The reduction does not seem to depend directly on the rickets. There are reasons for believing that in many instances the reduction is associated with a latent form of tetany.

The inorganic phosphorus of the serum is regularly reduced in active rickets, sometimes to an extreme degree.

During the process of healing, whether occurring spontaneously or as the result of the administration of cod liver oil, the phosphorus content of the serum gradually rises to a normal figure and often somewhat above this. Relapses are accompanied by a fall in the phosphorus concentration of the serum.

All the children under 2½ years of age, in whom we have found an inorganic phosphorus content of the serum of 3.0 mg. or less, have been suffering from active rickets.[36]

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36. While engaged in this work our attention was directed to a publication in the Forhandlingerne ved Første Nordiske Kongres for Paediatri, 1920, by Paul Iversen and Ejnar Lenstrup.[37] These authors studied the concentration of acid soluble, acid insoluble and total phosphorus in the whole blood and plasma of normal and rachitic infants. They found a low acid soluble phosphorus in children suffering from rickets compared with the normal. They also found an increase of the phosphorus after the administration of cod liver oil. Though the number of cases studied was small, and the diagnoses were not confirmed by roentgenograms, it appears that their results were quite similar to our own.

37. For the translation of this article we are greatly indebted to Professor Collitz of the Johns Hopkins University.

A CONTRIBUTION TO THE TOPOGRAPHIC ANATOMY OF THE THYMUS GLAND, WITH PARTICULAR REFERENCE TO ITS CHANGES AT BIRTH AND IN THE PERIOD OF THE NEW-BORN

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The peculiar life history of the thymus gland in man is reflected in its topography, which is modified from time to time by different phases of its growth and involution and by changes in the neighboring structures and viscera. These changes in thymus topography begin during fetal life and are particularly striking at birth when the chest and its contained organs are greatly modified as respiration is established. The natal changes of the thymus have received comparatively little study, and the lack of information on this subject seems to have led to considerable confusion regarding the normal form and extent of the organ in early postnatal life. The following account is an attempt to trace in detail these early modifications in thymus topography with particular reference to the normal or usual conformation and relations of the structure in early infancy. This work was done in the Department of Anatomy of the University of Minnesota under the direction of Dr. R. E. Scammon.

I. MATERIAL AND METHODS

The material used in this study consisted of sixty-five fetuses and full-term children. The specimens ranged from 10 to 55 cm. in crown-heel or total length. Most of these form a part of the collection of the Institute of Anatomy of the University of Minnesota. Twenty-five of the infants were stillborn and twenty were children in whom respiration had been at least partially established. Fifty-seven were preserved by intravascular injection of an aqueous solution of 10 per cent. liquor formaldehydi and 1 per cent. chromic acid, one was sectioned serially, and 7 were observed at the necropsy.

Following the suggestion of Hammar[1] that only thymus glands obtained from healthy individuals should be used in the study of this organ, no material was used in which pathologic conditions were macroscopically observable.

This material was studied by means of dissections, graphic reconstructions and freehand sections. The dissection of the first forty-two subjects in the series was made in the following manner; the skin, subcutaneous tissues, muscles, etc., were reflected from the anterior

1. Hammar, J. A.: Fünfzig Jahre Thymusforschung, Ergeb. Anat. u. Entwicke **19**: Pt. I, 274, 1909.

thoracic wall and the cervical region as far superiorly as the inferior border of the mandible. Next, the sternocleidomastoid and the infrahyoid muscles were removed and the part of the thymus extending above the sternal notch was measured with dividers. The ribs and clavicles were then cut at the anterior axillary lines, elevated and separated from their connections with underlying structures. In this manner the larynx, thyroid, thymus, pericardium, lungs, larger vessels, etc., of the mediastinum and cervical regions were exposed.

All measurements of these various structures as shown on the drawings were made with fine pointed dividers and were plotted on coordinate paper in the form of outline drawings of which several are reproduced in Figures 1 to 12 inclusive. Figures 19 to 24 inclusive were drawn from plottings of the anterior dissections which were made by the use of the graphic reconstruction apparatus designed by Scammon.[2] Fifteen specimens (Cases 43 to 58 inclusive, except Case 56) were cross sections prepared by sectioning the specimens free hand with a heavy, sharp knife. Figures 37 to 42 inclusive are drawings of selected specimens of this series. The 7 necropsies, which are included in the series (Cases 59 to 65 inclusive) did not afford ideal conditions for this work. However, measurements of these specimens were made with the dividers while the organs were in situ and the thymus glands carefully removed and placed on cotton pads in hardening fluid. The form was thus preserved, and the specimens were then drawn to standard size. These are shown in Figures 31 to 36 inclusive.

The following observations were made on each specimen:

(a) The location of the thymus, whether completely in the thorax or partly in the thorax and extending into the cervical region. This classification of location is that suggested by Coplin.[3]

(b) The lobation of the thymus, i.e., number of lobes observable macroscopically. This classification also follows Coplin.[3]

(c) The overlapping of the thymus on the right ventricle, i.e., to what extent, if any, the right or left portions of the thymus extended on this part of the heart.

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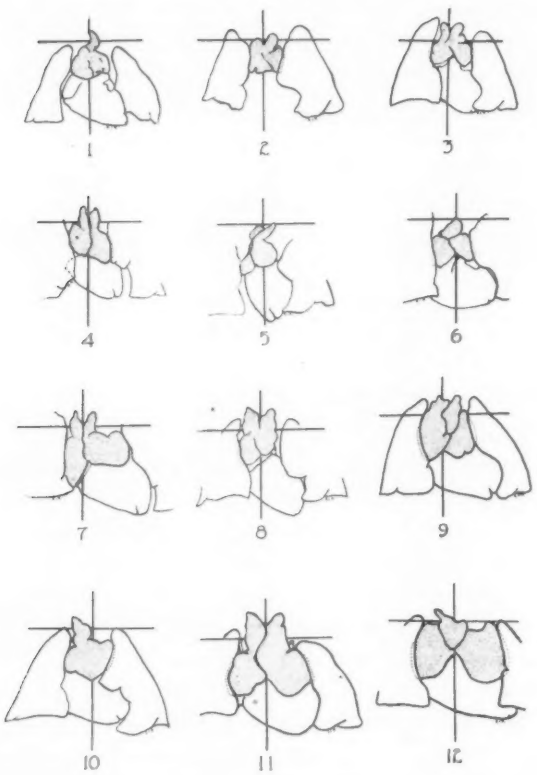
2. Scammon, R. E.: A Simple Method of Graphic Reconstruction, Anat. Rec. **21**:552, 1921.

3. Coplin, W. M. L.: Morphology of the Human Thymus. Pub. Jefferson Medical College and Hospital, **1**:116, 1915. Coplin suggests four different types of thymus glands in regard to lobation. He describes unilobar, bilobar, and trilobar glands which have respectively one, two or three lobes. Thymus glands in which division into lobes is imperfectly marked or in which fusion is so complete that no semblance of lobar distinction can be made out are classified as conglomerate. He found no thymus glands located entirely in the cervical region. I have likewise found none of this type in his material. A thoracic thymus is defined by Coplin as one of which the summit, under ordinary respiratory conditions, does not rise above the upper margin of the sternum. Cervicothoracic thymus glands are those of which continuous parts lie in the thorax and extend upward into the neck.



Figs. 1 to 12 represent outline drawings, plotted to scale, of a number of dissections in situ of thymus glands of fetuses and new-born children. None of these specimens had breathed.

Fig. 1.—Fetus 226 mm. in length (No. 12).
Fig. 2.—Fetus 234 mm. in length (No. 13).
Fig. 3.—Fetus 243 mm. in length (No. 15).
Fig. 4.—Fetus 245 mm. in length (No. 16).
Fig. 5.—Fetus 283 mm. in length (No. 18).
Fig. 6.—Fetus 235 mm. in length (No. 14).
Fig. 7.—Fetus 253 mm. in length (No. 17).
Fig. 8.—Fetus 374 mm. in length (No. 29).
Fig. 9.—Fetus 308 mm. in length (No. 22).
Fig. 10.—Fetus 300 mm. in length (No. 21).
Fig. 11.—Fetus 331 mm. in length (No. 25).
Fig. 12.—Fetus 384 mm. in length (No. 30).

(d) The overlapping of the thymus by the lungs, i.e., to what extent, if any, either or both lungs lay anterior to the thymus.

(e) The form of the thymus, i.e., whether the outline of the thymus was broad or elongate. A "broad" thymus was defined as one whose transverse diameter was equal to or greater than its craniocaudal diameter, and an "elongate" thymus as one whose craniocaudal diameter was greater than its transverse diameter.[4]

(f) Condition of the lungs in relation to respiration. The decision as to whether or not an individual had breathed was based on the floating test as well as on a careful examination of the lobules and the appearance of the anterior borders of the lungs with the hand lens. Lungs in which breathing has occurred show distinct characteristics when compared with those of the fetus or stillborn. The anterior border and antero-inferior angles of the former have lost their sharp edges and have become rounded. The lobules on the surface are larger, more distinct and of higher color. On section, the lungs in which respiration has begun appear spongy, and on pressure emit a frothy fluid containing numerous fine air bubbles. The latter phenomenon is noted in material which has been preserved for months as well as in fresh specimens. The extent and order of expansion of the parts of the lungs followed the observations of Champneys,[5] except that he found that the antero-inferior borders were often unexpanded.

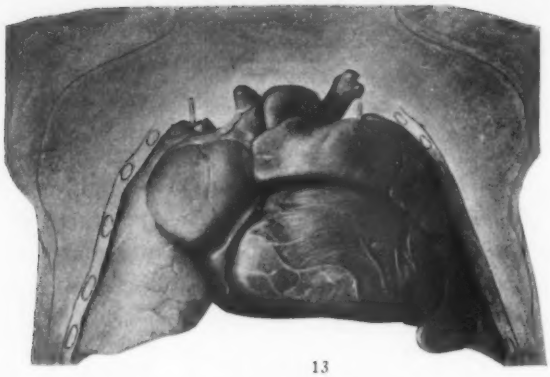
II. SUMMARY OF OBSERVATIONS

The data secured by the methods described above are summarized in Tables 1, 2 and 3. Since the series is arranged according to the crown-heel length of the specimens, one may quickly discern the changes occurring in any type of observation in relation to increase in body length and consequent age. Furthermore, the relation of the establishment of respiration to the various features observed may be noted by following the column allotted to the record of whether or not an individual had breathed. In the following analysis of these data the material will first be considered in toto and then as arranged in two series on the basis of the establishment or nonestablishment of respiration.

A. *Analysis of entire series of cases.*—A tabulation of the data obtained from the entire series of cases is shown in Table 1, and the following summary of the several observations is made from it.

4. A few thymus glands, because of their great lateral extension inferiorly, were classified as "broad" even though their craniocaudal diameters were a little greater than their transverse diameters—the former being due to the presence of slender cervical processes of some length.

5. Champneys, F. H.: Artificial Respiration in Stillborn Children, Med.-Chir. Tr. Lond. **64**:41, 1881.



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Figs. 13 to 18 represent a series of dissections of chests of new-born children illustrating the changes in the form of the thymus coincident with the establishment of respiration.

Fig. 13.—Anterior dissection of the thorax of a new-born which had breathed (No. 39, 485 mm. long). The thymus is still of the fetal type though it evidently was already compressed, as is shown by the cervical portion being forced against the thyroid gland. This cervical portion was 7 mm. in thickness.

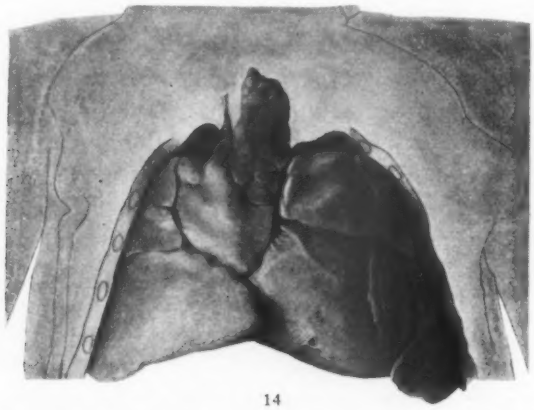

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Fig. 14.—Anterior dissection of the thorax of a new-born which had breathed (No. 40, 501 mm. long). The cervical portion of the thymus extended to the thyroid against which it was pressed, and then projected anteriorly. The anterior border of the right lung and the anterior-inferior angles of both lungs show the characteristic thickening in these areas in the earliest stages in the establishment of respiration.

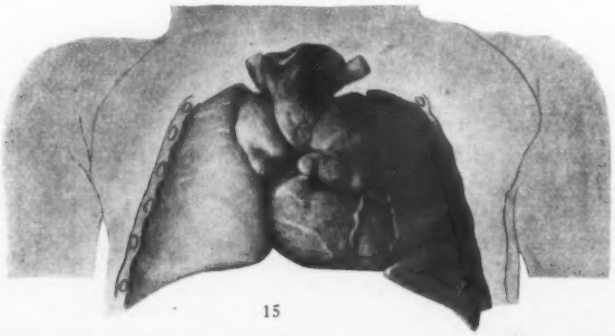

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Fig. 15.—Anterior dissection of the thorax of a premature new-born (No. 31, 402 mm. long) which had breathed. The thymus has a very wide cervical portion which extended to the inferior border of the thyroid gland against which it was compressed.

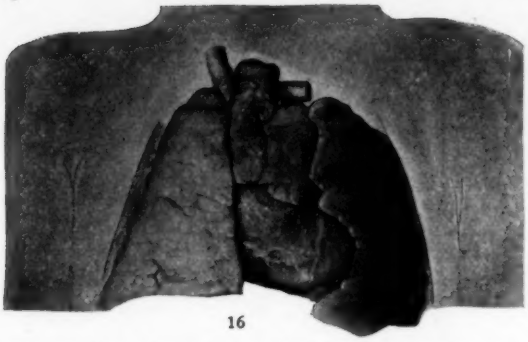

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Fig. 16.—Anterior dissection of the thorax of a premature new-born (No. 29, 374 mm. long) which had breathed. The thymus extended so far posteriorly that it compressed the innominate artery, trachea and esophagus. The thymus is markedly compressed from side to side, and the lobules of the lungs, anteriorly, are very marked. Figure 45 is of this specimen after the anterior half of the thymus was dissected away.

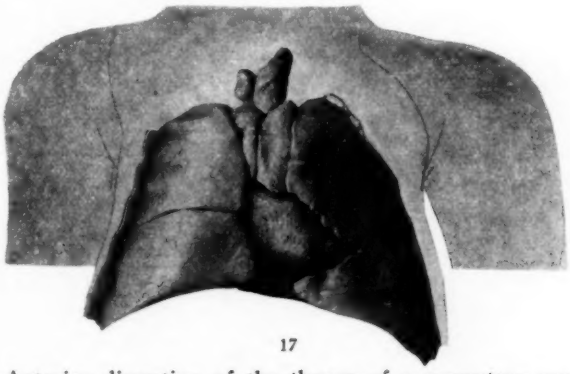

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Fig. 17.—Anterior dissection of the thorax of a premature new-born (No. 32, 412 mm. long) which had breathed. The cervical portion is quite large, and extends to the thyroid. The inferiormedial angles of the lungs have extended almost to the midline—the right lung practically reaching it.

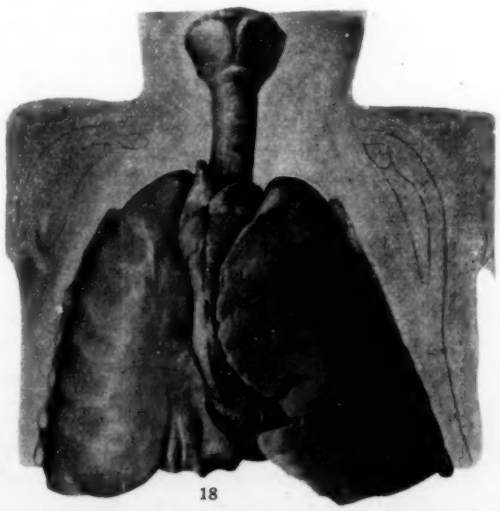

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Fig. 18.—Anterior dissection of the thorax of a newborn (No. 41, 510 mm. long) which had evidently breathed longer than any other in the series. The thymus is markedly compressed, the right lung has crossed the midline, and the left in its middle region has reached it. The thymus does not extend far into the cervical region, but it does extend very far down on the right ventricle. It is, like all the others, marked by a groove where it was in contact with the superior border of the manubrium sterni. Posteriorly, it compressed the aortic arch, innominate artery and trachea.

The predominating location of the thymus is cervicothoracic, this position being found in fifty-one cases, or 82.2 per cent. The thoracic location was found in eleven cases, or 17.8 per cent. The bilobed type of thymus predominates, with a total of thirty-nine cases, or 62.9 per cent. The conglomerate, trilobed, and unilobed thymus follow in frequency; the conglomerate with ten cases, or 16.1 per cent., the trilobed with seven cases, or 11.1 per cent., and the unilobed with six cases, or 9.9 per cent. The thymus was overlapped by the right lung in twenty cases, or 32.2 per cent., and by the left lung in eighteen cases, or 29 per cent. The right portion of the thymus overlapped the right ventricle in ten cases, or 16.1 per cent., and the left portion of the organ overlapped the right ventricle in seventeen cases, or 27.3 per cent. A broad thymus was present in forty-one cases, or 66.2 per cent., and an elongate thymus in twenty-one cases, or 33.8 per cent. The above figures are for the entire series and, therefore, include the individuals that have not breathed as well as those who have breathed.

B. *Analysis of cases in which respiration had not been established.*—When the individuals who have not breathed are considered as a separate group (Table 2) the following results are obtained.

The most frequent location of the thymus is cervicothoracic, with a total of thirty-six cases, or 80 per cent. The bilobed thymus is the most common in this group, forming 57.8 per cent. of the total number. The conglomerate type ranks next with nine cases, or 20 per cent., the unilobular numbers six cases, or 13.4 per cent., and the trilobed is least numerous, being represented by only four cases, or 8.8 per cent. The thymus is overlapped by the right lung in but three cases, or 6.6 per cent., and by the left lung in only two cases, or 4.4 per cent.

These figures indicate that in the nonbreathing individuals there is practically no overlapping of the thymus by the lungs. In no case in the nonbreathing group did the right portion of the thymus extend over the right ventricle of the heart, and the left portion projected on the right ventricle in only two cases, or 4.4 per cent. The broad type of thymus predominates in the nonbreathing group, with a total of thirty-seven cases, or 82.3 per cent. The elongate type occurs in only eight cases, or 17.7 per cent.

The individuals who have not breathed were also arranged into two subgroups according to total body length (Table 2). The first subgroup included all specimens of 30 cm. or less and contains twenty-one cases. The second subgroup includes all cases above 30 cm. and contains twenty-four cases. The lobation in both these groups is similar to the whole nonbreathing series, i.e., predominantly bilobed. The thoracic thymus is slightly more common in the second group. This may be interpreted as representing a stage in the migration of the thymus from its embryonic position in the cervical region to its final

TABLE 1.—Tabulation of the Several Observations Made on the Entire Series of Thymus Glands. Nos. 1 to 42, Inclusive, Were Dissections; Nos. 43 to 58, Inclusive, Were Transverse Sections, and Nos. 59 to 65 Were Necropsies

Series Number	Standing Height	Sex	Type of Thymus	Lobation of Thymus	Lungs Overlap Thymus		Thymus Extend on Ventricle		Form of Thymus	Breathed
					Right	Left	Right	Left		
1	100	F	C-T	Cong.	—	—	—	—	B	—
2	119	M	C-T	Bi.	—	—	—	—	E	—
3	123	F	Th.	Uni.	—	—	—	—	E	—
4	133	F	C-T	Bi.	—	—	—	—	E	—
5	143	M	Th.	Cong.	—	—	—	—	B	—
6	186	F	C-T	Uni.	—	—	—	—	E	—
7	200	F	C-T	Bi.	—	—	—	—	E	—
8	220	F	C-T	Bi.	—	—	—	—	B	—
9	223	F	C-T	Bi.	—	—	—	—	B	—
10	223	M	C-T	Tri.	—	—	—	—	E	—
11	224	F	C-T	Bi.	—	—	—	—	B	—
12	226	M	C-T	Cong.	—	—	—	—	B	—
13	234	F	C-T	Cong.	—	—	—	—	B	—
14	235	M	Th.	Tri.	—	—	—	—	B	—
15	243	F	C-T	Bi.	—	—	—	—	B	—
16	245	M	C-T	Bi.	—	—	—	—	B	—
17	253	F	C-T	Bi.	—	—	—	—	B	—
18	283	M	C-T	Bi.	—	—	—	—	E	—
19	283	F	C-T	Bi.	—	—	—	—	E	—
20	295	F	C-T	Tri.	—	—	—	—	B	—
21	300	F	C-T	Uni-	—	—	—	—	B	—
22	308	F	C-T	Cong.	—	—	—	—	B	—
23	313	F	C-T	Cong.	—	—	—	—	B	—
24	325	M	C-T	Bi.	—	—	—	—	B	—
25	331	F	C-T	Bi.	—	—	—	+	B	—
26	332	M	C-T	Bi.	—	—	—	—	B	—
27	337	F	C-T	Bi.	—	—	—	+	B	—
28	364	F	C-T	Cong.	+	+	—	+	B	—
29	374	F	C-T	Tri.	+	+	+	+	E*	+
30	384	F	C-T	Tri.	—	—	—	+	B	—
31	402	F	C-T	Tri.	+	+	+	+	B†	+
32	412	F	C-T	Bi.	+	+	+	+	E	+
33	421	M	C-T	Cong.	+	+	+	+	E†	+
34	402	F	C-T	Bi.	+	+	+	+	E*†	+
35	433	F	C-T	Cong.	—	—	—	—	B	—
36	448	F	Th.	Bi.	—	—	—	—	B	—
37	453	F	C-T	Bi.	—	—	—	—	B	—
38	470	F	Th.	Bi.	+	+	—	—	B*	+
39	485	M	C-T	Bi.	+	—	—	+	B*	—
40	501	F	C-T	Tri.	+	+	+	+	B*†	+
41	510	F	C-T	Bi.	+	+	+	+	E*	+
42	516	F	C-T	Cong.	—	—	—	—	B	—
43	295	F	C-T	Uni.	—	—	—	—	B	—
44	310	F	C-T	Bi.	+	+	—	+	E	+
45	320	M	C-T	Bi.	—	—	—	—	B	—
46	340	F	Th.	Bi.	—	—	—	—	B	—
47	360	F	C-T	Bi.	—	—	—	+	B	—
48	370	M	C-T	Bi.	—	—	—	—	B	—
49	373	M	Th.	Bi.	—	—	—	—	B	—
50	375	F	C-T	Bi.	+	+	—	—	E	+
51	380	M	C-T	Bi.	+	+	+	+	E	+
52	380	F	C-T	Bi.	+	+	+	+	E	+
53	382	M	C-T	Bi.	+	+	+	+	E	+
54	410	M	C-T	Bi.	—	—	—	—	B	—
55	420	F	C-T	Bi.	—	—	—	—	B	—
56	430	F	C-T	Bi.	+	—	—	—	E	+
57	480	M	Th.	Uni.	—	—	—	—	B	—
58	510	F	Th.	Bi.	—	—	—	—	B	—
59	370	F	C-T	Bi.	+	+	—	—	B	+
60	515	F	C-T	Bi.	—	—	—	—	B	—
61	305	F	C-T	Bi.	+	+	—	+	E	+
62	450	M	Th.	Bi.	+	+	—	+	E	+
63	14 mo.	F	Th.	Bi.	+	+	+	+	E	+
64	510	M	C-T	Bi.	+	+	+	—	B	+
65	550	F	C-T	Cong.	+	+	+	—	E	+

* Constriction or flattening of structures posterior to thymus.
† Cervical part of thymus very large.

position in the thorax in postnatal life.[6] There is no overlapping of the thymus by the lungs in the first group, and but a few instances of slight overlapping in the second group which are probably due to the inclusion of a few individuals suspected of having breathed slightly. The thymus in no case in the first group extends on either side on the right ventricle. In the second group the thymus in a few cases extends

TABLE 2.—CONDITION OF THE THYMUS IN INDIVIDUALS WHICH HAVE NOT BREATHED

	Specimens 100 to 300 Mm. in Length (21 Cases)		Specimens 300 to 315 Mm. in Length (24 Cases)	
	Number	Per Cent.	Number	Per Cent.
Lobation of Thymus				
Unilobar	3	14.3	2	8.3
Bilobar	11	52.4	16	66.7
Trilobar	3	14.3	1	4.1
Conglomerate	4	19.0	5	20.9
Position of Thymus				
Cervicothoracic	18	85.7	19	79.1
Thoracic	3	14.3	5	20.9
Lungs Overlap Thymus				
Right side	0	0.0	2	8.4
Left side	0	0.0	1	4.2
Thymus Extends on Ventricle				
Right side	0	0.0	1	4.2
Left side	0	0.0	4	16.7
Form of Thymus				
Broad	13	61.9	24	100.0
Elongate	8	38.1	0	0.0

TABLE 3.—EFFECT OF THE ESTABLISHMENT OF RESPIRATION ON THE THYMUS

	Individuals Which Have Not Breathed		Individuals Which Have Breathed	
	Number	Per Cent.	Number	Per Cent.
Position of Thymus				
Cervicothoracic	36	80.0	16	80.0
Thoracic	9	20.0	4	20.0
Lobation of Thymus				
Unilobar	6	13.4	0	0.0
Bilobar	26	57.8	15	75.0
Trilobar	4	8.8	3	15.0
Conglomerate	9	20.0	2	10.0
Lungs Overlap Thymus				
Right side	3	6.6	20	100.0
Left side	2	4.4	16	80.0
Thymus Extends on Ventricle				
Right side	0	0.0	13	65.0
Left side	2	4.4	16	80.0
Form of Thymus				
Broad	37	82.3	5	25.0
Elongate	8	17.7	15	75.0

on the left ventricle; this is probably due to slight breathing. Less than two-thirds of the cases in the first group have the broad type of thymus, whereas every case in the second group has the broad thymus.

C. *Analysis of cases in which respiration was partially or wholly established.*—The findings regarding the thymus in the group of cases in which respiration was partially or wholly established are given in Table 3.

6. Canelli, H. K.: Contributo allo studio anatomico e pathologico dell timo nella prima eta, Pediatria **28**:753, 1920.

The most common position of the thymus in individuals who have breathed, as in the entire series, is the cervicothoracic with a total of sixteen cases, or 80 per cent. The thoracic location is found in but four cases, or 20 per cent. The bilobed type of thymus predominates in this group with a total of fifteen cases, or 75 per cent. The trilobed type is next in order with three cases, or 15 per cent. The conglomerate is represented by but two cases, or 10 per cent., and there are no unilobed thymus glands present in this group.

These results in regard to lobation agree, in the main, with the findings of most other observers in that the bilobed type is generally described as being the most prevalent.

The thymus is overlapped by the right lung in all members of this group. It is overlapped by the left lung in sixteen, or 80 per cent. of the cases.

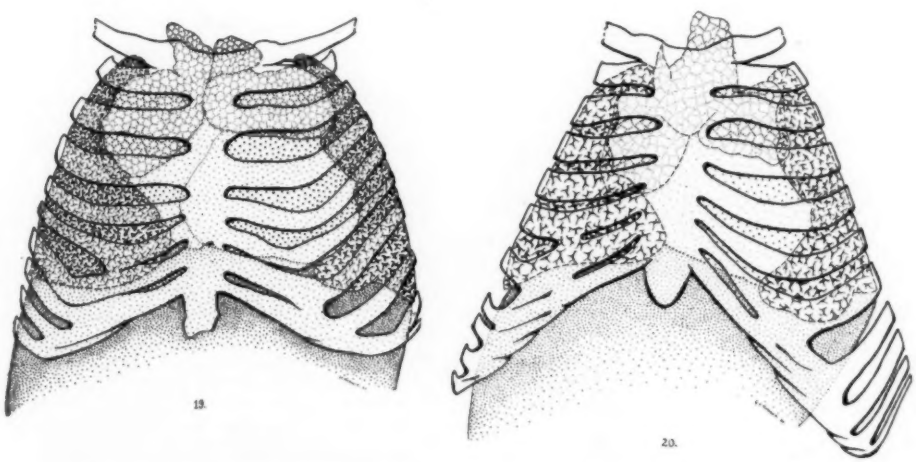


Fig. 19.—A graphic reconstruction of No. 39 (485 mm. long) which is also shown in Figure 2. The overlapping of the thymus by the lung, extent of cervical portion of the thymus, and relation of thymus to sternum and ribs are shown in this and the following graphic reconstructions.

Fig. 20—Graphic reconstruction of No. 40 (501 mm. long) which is also shown in Figure 3.

The right portion of the thymus extends on the right ventricle of the heart in thirteen cases, or 65 per cent. of this group. The entire series shows but 16.1 per cent. and the nonbreathing group shows not a single case.

The left portion of the thymus extends on the right ventricle in sixteen cases of this group, or 80 per cent. The nonbreathing group shows but 4.4 per cent.

The broad type of thymus occurs in but five cases, or 25 per cent. in this group, and the elongate thymus in fifteen cases, or 75 per cent.

III. DISCUSSION

A. *The Fetal Thymus and its Transformation in the Neonatal Period.*—From the observations recorded above it is seen that the thymus in the latter part of fetal life is quite constant in its form, and in its relation to other organs and structures in the thoracic and cervical regions. Its location may be either thoracic or cervicothoracic with the latter location the more frequent (i.e., in about four out of five cases). The organ is distinctly broad in outline, extending laterally as far as the anterior axillary lines in most cases. The number of lobes in the majority of cases is two—this type of lobation being substantially the same as is found in postfetal life. The fetal thymus is practically never overlapped by either lung, thus leaving its anterior surface directly in contact with the posterior surface of the anterior chest wall.

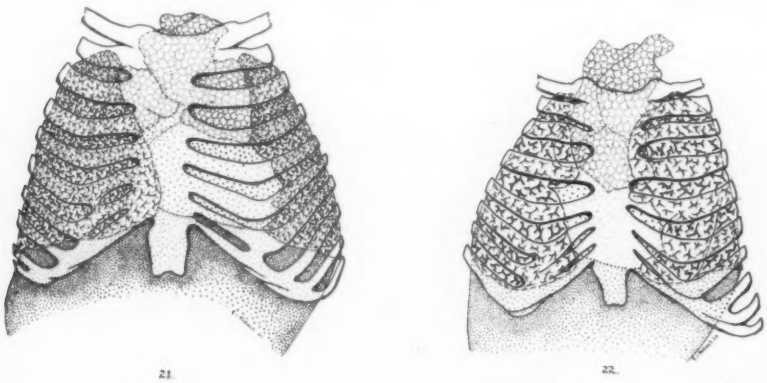


Fig. 21.—Graphic reconstruction of No. 31 (402 mm. long) which is also shown in Figure 4. The extension of the thymus over the ventricle on the left side is clearly shown. The right lung has almost reached the midline, but the anterior margin of the left lung is still a great distance from it.

Fig. 22.—Graphic reconstruction of No. 34 (401 mm. long) which is also shown in Figure 6. The overlapping of the thymus by both lungs, and the extent of the thymus inferiorly on the right ventricle is well shown.

Inferiorly, the organ does not extend, on either side, on the surface of the right ventricle of the heart. The probable explanation of the broad type of thymus in late fetal life lies in the constant increase in the relative weight of this organ during the last few months before birth. This fact is clearly brought out by the collected data on the weight of the fetal thymus recorded in this laboratory.

The distinctly broad type of thymus described above as being of the fetal type is also found to be typical of full term stillborn children. This is shown in Figure 31 (No. 60 of the series) of the thymus of a full term stillborn child. The lungs in this case did not extend on the anterior surface of the thymus nor did this organ show any evidence of molding.

The thymus in the infant in which respiration has been partially or wholly established, like that of the late fetus, is usually cervicothoracic in location and is also, in most of the cases, composed of two lobes. But it is elongate in form and bears the impress of the organs with which it is in contact. The right lung extends on its anterior surface in every case and the left lung extends over its anterior surface in four out of five cases. The thymus overlaps the right ventricle of the heart on the right side in more than 50 per cent. of the cases, and on the left side in over three-fourths of these individuals.

The transition from the broad or fetal type to the elongate and molded type of thymus found in the individuals who have breathed is accomplished during the time in which respiration is completely estab-

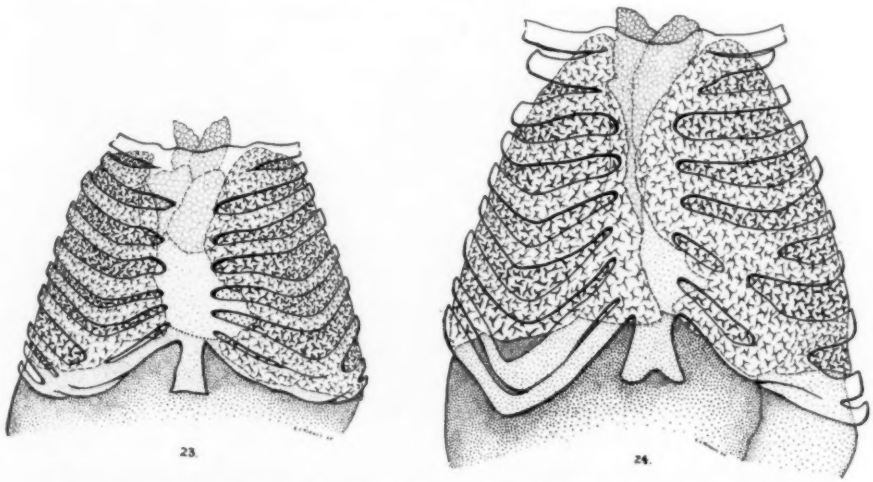


Fig. 23.—Graphic reconstruction of No. 32 (412 mm. long). The anterior dissection is shown in Figure 7.

Fig. 24.—Graphic reconstruction of No. 41 (510 mm. long) also shown in Figure 8. The extent of thymus overlapped by the lungs is indicated by the broken line. The cervical portion of the thymus, and the relation of the thymus to the ribs and sternum are clearly shown in this drawing. The longitudinal axis of the heart, in this case, is much more nearly vertical than in any of the other individuals in the series. It will also be noted that the anterior-inferior angles of both lungs extend slightly below the angle of the costal arch. The outline of the thoracic cage, on comparison with the cases which have breathed less, shows that it has become more narrow and ovoid in shape.

lished. The expansion of the lungs changes the position and relations of the thoracic contents, and along with the other organs and viscera of the thorax the thymus is markedly affected. It is compressed both laterally and anteroposteriorly, with the resultant elongation and molding, and extension over the right ventricle.

The thymus glands of infants who have breathed a very short time show but little change in form or relations from the broad or fetal type. This is well shown in Figure 33 (No. 65); (congenital cystic kidneys). This infant had lived half an hour, and in that time the thymus was but very slightly molded. The right lung overlapped the thymus slightly as did also the left lung. The thymus was flattened on the left side but not at all on the right. The right lobe was very large and extended posteriorly to a marked extent. On making the floating test, it was found that only a small part of the right lung floated, whereas the entire left lung did so. I am inclined to believe that the very large right lobe of the thymus compressed the bronchus, thus interfering with the expansion of the right lung.

The molding of the thymus seems to be quite closely related with time in the neonatal period. This is well shown in Figures 31 to 36, inclusive. The thymus of an infant which had lived four hours (cerebral hemorrhage) is reproduced in Figure 32 (No. 64). In this case the thymus was overlapped by both lungs and was molded by them. The organ also extended on the right ventricle on the right side. Figure 34 is a drawing of series number 61, a premature (whose abortion was induced by overactivity on the part of the mother) which had lived twelve hours. The lungs overlapped the thymus on both sides, distinctly molding the organ so that it presents lateral depressions. On the left side the thymus extended slightly on the right ventricle. It resembles closely number 31 of the series, as may be seen on comparing it with Figures 15 and 26. The thymus of an infant which had breathed twenty-six hours (diabetic mother; cesarian section) is shown in Figure 35. It is number 62 of the series. In this case the lungs overlapped the thymus on both sides, flattening and making definite impressions on them. The thymus is elongated and extended on the right ventricle on the left side. This specimen is very similar to that of number 29, as may be seen on comparison with Figures 16 and 25. The thymus of a 14 months old child was found to be of the elongated type, very thin, and convexly molded by the lungs which completely covered the organ. It corresponds to those usually described for young children and is similar to the figures by Spalteholz [10] of a 12 year old boy.

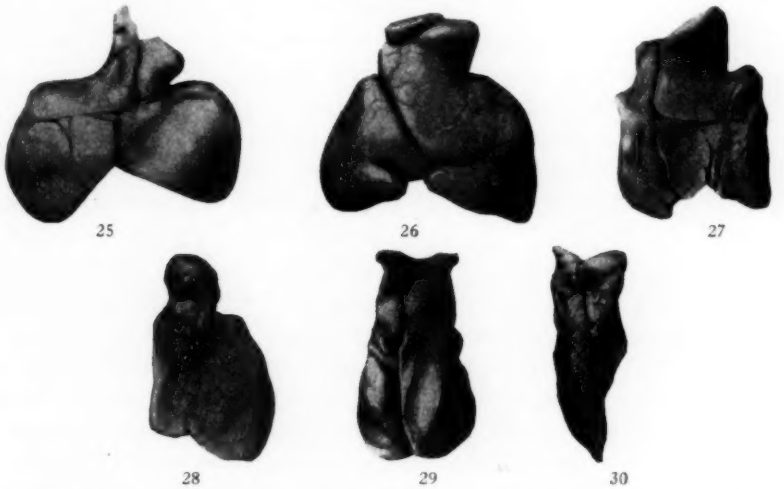
It may, therefore, be said, in general, that the thymus glands observed at necropsy, taken as a group, indicate that the molding and changes in relations of the organ agree with those found in my cadaver series, and that these changes take place very early in life—in fact, during the neonatal period.

Several thymus glands which were removed from individuals who had breathed were drawn to a standard size; these are shown as Figures

25 to 30, inclusive. All in this group are from the cases in which anterior dissections were drawn, except Figures 27 and 29.

This series of drawings shows various degrees of molding of the thymus which correspond with the extent of expansion and consequent compression by the lungs. The transition in form from the broad fetal or stillborn type to the markedly molded and elongated type found in the individuals who have breathed, is readily seen in this group. Most of these thymus glands show a grooving at the level of the sternal notch, thus indicating that the pressure at this point must have been very great.

B. *The Relation of the Thymus to the Anterior Skeletal Wall.*—The relation of the thymus to the anterior skeletal wall in the late fetal



Figs. 25 to 30 represent a group of thymus glands drawn to standard size illustrating the effect of the establishment of respiration on the form of the thymus.

Fig. 25.—Thymus from Case 39, also shown in situ in Figure 13. This specimen shows a slight molding by the overlapping lungs. Crown-heel length of this specimen 485 mm.

Fig. 26.—Thymus from Case 31 (402 mm. long) shown in situ in Figure 15. The compression by the lungs is here shown by the lateral molding and the anterior depression underlying the sternal notch.

Fig. 27.—Thymus from a full term liveborn infant. Marked molding due to compression by the lungs and a depression at the level of the upper border of the manubrium sterni is well shown.

Fig. 28.—Thymus from Case 29 (374 mm. long) shown in situ in Figure 5. The flattened sides and depression by the upper border of the manubrium sterni are well shown.

Fig. 29.—Thymus of a liveborn infant showing very marked lateral compression; this figure also shows the groove made by the upper border of the manubrium sterni.

Fig. 30.—Thymus from Case 41 (510 mm. long) shown in situ in Figure 18. The marked impression on the left and molding on the right side are well shown. A conception of the great sagittal extent of the organ may be obtained from this picture.

stages and in the new-born may be seen in Figures 19 to 24, inclusive. These are graphic reconstructions of Nos. 39, 40, 31, 34 and 41 of my series. These specimens are also shown in Figures 13 to 18, inclusive.

The degree of expansion of the lungs influences the extent of the thymus lateral to the borders of the sternum and also the extent of the thymus inferiorly. In the late fetus and in the stillborn the thymus extends as far laterally as the anterior axillary line. In cases of slight breathing, it was noted that it was the right lung which had made the greatest advance toward the median line, and that the thymus on this side was less extensive than on the left. The inferior limits of the thymus in the stillborn was, in most cases, at the upper border of the fourth costal cartilage with but a few as low as the upper border of the fifth costal cartilage. In the individuals who had breathed, the lateral extent of the thymus was slight, and occasionally not at all on one side. The inferior limit of the thymus in these cases was, as a rule, somewhat lower. A few were at the level of the upper border of the fourth costal cartilage, but those whose lungs were well expanded extended as far inferiorly as the upper border of the sixth costal cartilage.

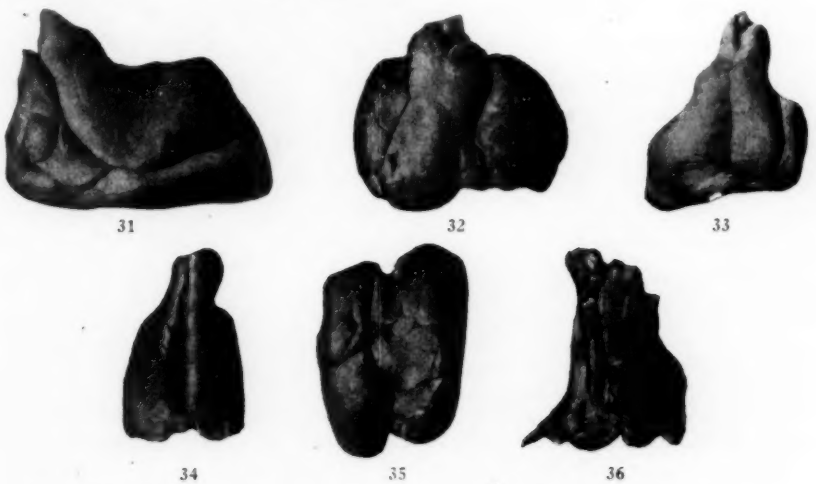
In general, the outline of the thymus on the anterior chest wall is described in the literature as a triangular area with the base extending horizontally from one sternoclavicular joint to the other. The sides of the triangle extend inferiomedially from these joints to the level of the second, third or fourth rib—the latter limit varying with different authors. It is held that a thymus lying within the above limits is of normal size, and that if the thymus extends lateral to the sides of the triangle it is probably enlarged. This enlarged or hypertrophied thymus is then suspected of exerting pressure on the structures adjacent to it.

The findings here presented indicate that in the neonatal period, the degree of expansion of the lungs is a more potent factor in determining the lateral extent of the thymus than is the actual size of this organ. In this connection it may be pointed out that during the period of the new-born at least, a thymus lying within the usually described normal area may exert marked pressure on the structures posterior to it. This is the condition which was present in No. 41 of my series of cases. Figure 24 is a drawing of the graphic reconstruction of this case; Figure 18 is from the anterior dissection, and Figure 30 is of the thymus after removal. (See also Figure 45 which shows another case in which the greater part of the thymus has been removed.) I believe as Warthin [7] points out, that the anteroposterior extent of

7. Warthin, A. S.: Pathology of Thymic Hyperplasia and Status Lymphaticus, Arch. Pediat. **26**:597, 1919.

the organ as well as its transverse extent is an important point in determining whether or not a thymus is enlarged.

C. *The Posterior Relations of the Thymus.*—The posterior relations of the thymus are in a measure determined by its craniocaudal diameter. A cervicothoracic thymus may extend far into the neck and meet the inferior border of the thyroid, as is the case in Nos. 34 and 40 of my series. In these cases the thymus, after coming in contact with the inferior border of the thyroid, turned anteriorly and laterally. On the other hand, the thymus may extend inferiorly to such an extent that it will lie on the right ventricle.



Figs. 31 to 45 represent a series of thymus glands secured at necropsy and hardened by immersion in chrome-formol. The form of the specimens was preserved by mounting them on pads of cotton.

Fig. 31.—No. 60 (315 mm. long) full term stillborn.

Fig. 32.—No. 64, full term infant which had lived four hours.

Fig. 33.—No. 59 (370 mm. long) premature infant.

Fig. 34.—No. 61 (305 mm. long) premature which lived twelve hours.

Fig. 35.—No. 62 (450 mm. long) new-born infant which had lived twenty-six hours.

Fig. 36.—No. 63. Thymus of a 14 months old girl. This thymus was markedly molded and compressed. Its anterior-posterior diameter was but 4 mm.

The thymus in late fetal life and in the new-born is related posteriorly to the pericardium over the base of the heart and great vessels. On the left it may extend, in exceptional instances, as in one of this series, to the left vagus nerve. On the right it is generally found to be applied closely to the superior vena cava. The left innominate vein, and, occasionally, the superior vena cava, is embedded in the posterior aspect of the thymus. In a few cases it was found that these vessels actually ran through the substance of the gland. The innominate artery is closely applied to the trachea and crosses it diagonally, and the left

innominate vein passes across the artery at the level of the upper border of the sternum. An increase in the anteriorposterior extent of the thymus in this region would, due to the rigidity of the superior thoracic aperture, compress the above named structures. In several of my cases this had evidently occurred. In these specimens the innominate artery was so greatly compressed against the trachea that it left a definite furrow marking its course across this tube thus

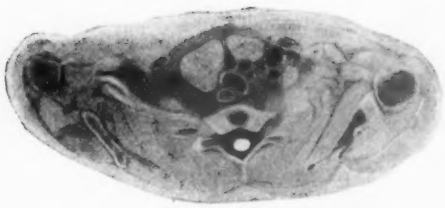


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Fig. 37.—Cross section of No. 51 (380 mm.) through the cervical region just above the sternal notch; the thymus is bilobed.

Fig. 38.—Cross section of the thorax of a full term fetus 510 mm. long (stillborn), below the sternal notch and above the aortic arch, showing the broad type of thymus. It will be noted that the innominate vein passes through the thymic substance to join its fellow, and that the thymic substance extends posteriorly as far as the posterior wall of the esophagus.

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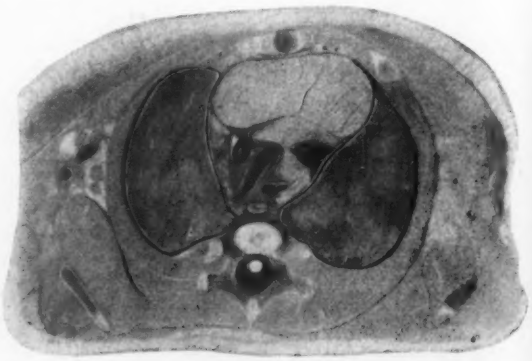

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Fig. 39.—Cross section of the thorax of a new-born infant 410 mm. long. This section shows a broad thymus with a rather extensive anteriorposterior diameter.

Fig. 40.—Cross section of the thorax of a stillborn full term fetus (480 mm.). This shows the characteristic broad type of thymus found in the late fetus and stillborn. This section is at the level of the aortic arch and shows a very marked posterior prolongation of the thymus. The convex sides of the thymus, characteristic in the stillborn, is well illustrated here. An evident constriction of the trachea due to partial surrounding by thymic substance is clearly shown.

markedly reducing the lumen. In one case the esophagus was in turn compressed by the trachea so that its right border was reduced to knife-edge while its left border was rounded. In another case, the esophagus had a marked dilatation on the right side just superior to the constriction. In still another case the thymus posteriorly partially enveloped the arch of the aorta so that the transverse diameter of this vessel was only half its anteriorposterior diameter (Fig. 45).

The thymus may not only compress the structures that lie posterior to it, but portions of it may project posteriorly and thus interfere with the structures there situated. An example of this is shown in Figures 43 and 44, which were drawn from series No. 27. This infant, according to the criteria used, had not breathed. The superior portion of the thymus extended posteriorly between the innominate artery and the left common carotid until it pressed against and constricted the trachea. The thymus must have compressed the left innominate vein a little lower so that the artery, in turn, was flattened against the

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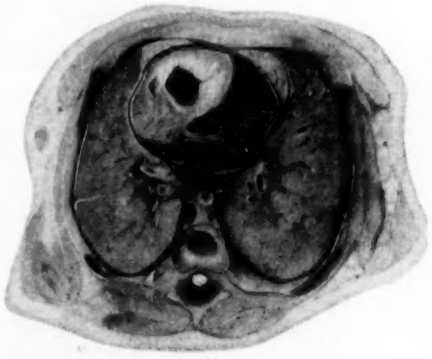

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Fig. 41.—Cross section of the thorax of an eight month stillborn fetus (No. 54, 410 mm.) through the level of the aortic arch. This figure shows an isolated portion of the thymus situated between the superior vena cava and the beginning of the tracheal bifurcation. At a higher level this small portion was continuous with the main mass of thymus.

Fig. 42.—Cross section through the atria and the right ventricle of the heart of a new-born infant. The thymus in this case passes over the right atrium and extends on the right ventricle. The flattened left lateral surface, the overlapping by the right lung, and the extent of the thymus on the right ventricle would indicate that this individual had breathed.

trachea with the consequent constriction of the latter structure. The esophagus in this region in cross-section was somewhat triangular in outline with the sharp apex lying under cover of the trachea. Figure 44 shows the deep groove in the anterior wall of the trachea. This groove was situated just above the level of the sternal notch which thus emphasizes the fact that in the late fetus and in the stillborn the tracheal bifurcation is much nearer the sternal notch than in later life.

The cross sections, several of which are here reproduced, are also instructive from the point of view of posterior relations of the thymus.

A section through the cervical region just above the sternal notch is shown in Figure 37. The thymus in this specimen was bilobed and extended posteriorly on the left as far as the anterior surface of the esophagus. It was also slightly in contact with the left lateral surface of the trachea.

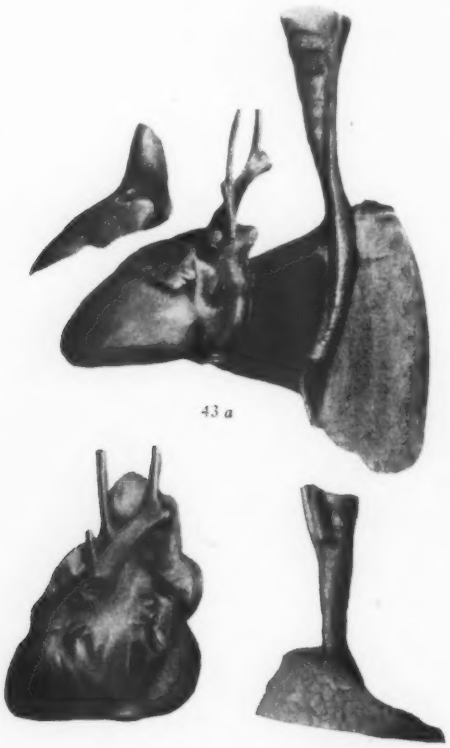

Fig. 43.—Drawings of Case 27 (premature, 337 mm. long) showing compression of structures posterior to the thymus. (*a*) The molded thymus, compressed great vessels, trachea and esophagus are shown in their relative positions. The thymus shows the grove for the left innominate vein and a posterior-superior knoblike process which projected between the innominate artery and left common carotid and against the trachea which it compressed. The innominate artery is seen to be flattened by the thymus—and in turn compressed the trachea. (*b*) Posterior view of thymus, heart and arteries. (*c*) Lateral view of the compressed trachea showing the markedly flattened right border of the esophagus.

A section through a lower level, i.e., through the manubrium sterni and above the aortic arch of a full term fetus is shown in Figure 38. It shows a broad thymus through which the left innominate vein passed as it joined its fellow forming the superior vena cava. It seems logical to assume from this relation that marked congestion or compression

of this thymus would lead to a cyanotic condition of the head, neck and upper extremities. The greater posterior extent of the thymus in this case is on the left side and a tongue-like process extends as far backward as the posterior wall of the esophagus. It is also in contact with the right side of the trachea and has evidently compressed the innominate artery and the trachea to a slight degree.

Figure 39 is of a section through the level of the tracheal bifurcation of a stillborn child. The thymus here is of the broad type with a marked anteriorposterior diameter. On the left side, the thymus is seen to extend even posterior to the trachea though it is not in direct contact with it. On the right side, the anterior surface of the superior vena cava is in direct contact with the thymus and is partially enveloped by it.

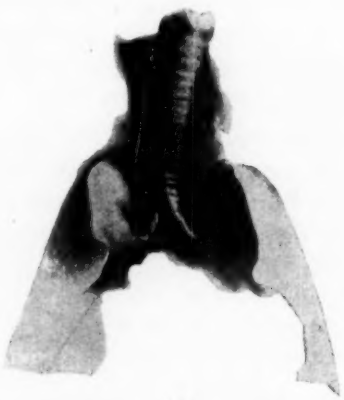

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Fig. 44.—No. 27 (premature 337 mm. long), anterior view of the compressed trachea showing the diagonal course of the innominate artery, as is indicated by the furrow the artery has made on the trachea.

Fig. 45.—Drawing of Case 29 (premature 374 mm. long). The greater part of the thymus has been removed and only enough left so as to show its extent posteriorly. The thymus encloses the aortic arch. The oblique course of the innominate artery as well as its impression on the anterior surface of the trachea is shown.

A section at a lower level—through the arch of the aorta of a stillborn child is shown in Figure 40. We have here a very broad thymus which in this case extends posteriorly to a very great degree. It is seen projecting between the arch of the aorta and the superior vena cava and continues posteriorly as far as the anterior surface of the esophagus. This thymus bears a medial indentation into which fitted the right third of the tracheal bifurcation.

Figure 41 (stillborn child) is also a cross section through the tracheal bifurcation but at a lower level than the preceding one. It has the broad type of thymus with the lungs not extending over the anterior aspect of the former. This thymus is noteworthy, due to the

posterior projection which is here shown as an isolated mass. This mass was continuous with the main part of the thymus at a higher level. At this level it is situated between the superior vena cava and the tracheal bifurcation.

A transection through a much lower level (Figure 42, through the heart) shows the thymus extending on the right ventricle on the left side and the overlapping of the right atrium on the right side. The left lung does not extend on the anterior surface of the thymus but the right lung does so slightly, thus indicating that this individual had breathed at least to a limited extent.

D. *Form and Topography of the Thymus in Infancy and Childhood as Described in the Literature.*—The descriptions and figures of the thymus which are presented in the various texts, atlases and clinical publications give little indication of the changes in form and relations which the organ undergoes in the neonatal period. This is true despite the fact that the literature contains many figures of "new-born" thymus glands which vary widely in size, form and relations.

Applying the same criteria to descriptions and figures of the thymus glands in the literature as was used for the material presented here, it is possible to discern the same two general types, i.e., broad and elongate. At least three-fourths of the descriptions and illustrations of the thymus in the new-born conform to the type designated as "broad." [8]

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8. Cooper, A.: The Anatomy of the Thymus Gland, American Edition, Philadelphia, 1845.

Luschka, H.: Die Anatomie des Menschen, 1863, Tübingen **2**:324, et seq., Figure 26.

Mettenheimer, H.: Topographische Anatomie der Brust des neugeboreneu Kindes, Morphol. Arbeit. **3**:302 et seq., 1894.

Gegenbaur, C.: Lehrbuch der Anatomie des Menschen, Ed. 6, 1896, **2**:123, Figure 463.

Chievitz, J. H.: Topographical Anatomy of a Full-Term Human Fetus in Situ, Copenhagen, 1899, Figure 7.

Zuckerkandl, E.: Atlas der Topographischen Anatomie des Menschen, 1914, p. 244, Figure 288.

Sobotta, J.: In Bardeleben, Handbuch der Anatomie des Menschen, pp. 116, 122, 129; Figures 3, 9, 13; 1914.

Fetterolf, G., and Gittings, J. C.: Some Anatomic Features of the Child's Thorax, Am. J. Dis. Child. **1**:6 (Jan.) 1911.

Cunningham: Textbook of Anatomy, Ed. 4, 1913, pl. 1349, Figure; 1059.

Quain-Schaeffer: Elements of Human Anatomy, Ed. 11, 1914, **2**:2, p. 325.

Rauber-Kopsch: Lehrbuch der Anatomie, 1914, **4**: p. 236, Figure 289.

Coplin, W. M. L.: loc. cit.

Hammar, J. A.: Gewisse Fälle von Thymus Asthma im Lichte der Thymustopographie, Ztschr. f. Kinderh. **13**:226 et seq., 1915; Figures 4, 5, 6.

Sjollander, A., and Strandberg, A.: Om nerverna till thymus, Upsala Läkareförenings Forhandlingar **20**:244, 1915.

Gray-Lewis: Anatomy of the Human Body, 1920, p. 1273, Figure 1178.

I found but three instances in the literature in which the thymus of the new-born is described as elongate, and only three illustrations which show this form of thymus at birth.[9] The descriptions and illustrations of thymus glands in individuals one month and older are all of the elongate type.[10] All of the broad type thymus glands in the literature have corresponding cases in the present series. Since they are of this type, and are not at all overlapped or molded by the lungs, and have counterparts that have not breathed, I conclude that they are from stillborn individuals.

The above mentioned illustrations and descriptions from the literature show clearly the use of both broad and elongate types in descriptions of the thymus in the "new-born." In some cases terms such as "fetus at term," "full term fetus," [11] etc., are used. In the latter, the thymus glands illustrated or described are evidently from liveborn individuals.

These terms are confusing, and it seems that the terms "stillborn" and "liveborn" would be more appropriate in describing organs in the new-born since it is evidently to the living that the information will be applied.

I have been able to find but three references in the literature which indicate that the establishment of respiration has any possible connection with the form and relations of the thymus. Sappey [12] states that the thymus in the infant which has not breathed is of large size, thus suggesting the broad type. Hammar [13] in discussing the thymus in the new-born describes it as a distinctly wide organ whose lateral sur-

9. Huntington, G. S.: Topographic Anatomy of the Thorax in the Fetus at Term. Report New York Lying-In Society, 1897, New York.
Poirier and Charpy: Traite d'anatomie humaine, Ed. 2, 1911, **4**:568, Figure 304.
Testut and Jacob: Traite d'anatomie topographique, Ed. 2, 1909, **1**:839, 840, Figures 592, 593.
Corning, H. K.: Lehrbuch der topographische Anatomie, Ed. 3, 1911, p. 304, Figure 237.
Bardeleben, K.: Atlas der topographische Anatomie des Menschen, 1906, p. 63, Figure 118.
Morris-Jackson: Textbook of Human Anatomy, Ed. 5, 1914, p. 1320, Figure 1074.

10. Joessel, J.: Lehrbuch der Topographische Chirurgischen Anatomie, Bonn. Ed. 2, 1899, p. 74, Figure 16.
Piersol, G. A.: Anatomy of the human body, Philadelphia, 1908, p. 1273, Figure 1178.
Olivier, M. E.: Anatomie topographique et chirurgie du thymus, Thèse Par., 1911.
Sobotta, J.: In Bardeleben. loc. cit.
Spalteholz, W.: Handatlas der Anatomie des Menschen, Ed. 3, 1920.

11. Huntington, G. S.: loc. cit.

12 Sappey: Traite d'anatomie descriptive, Ed. 4, Paris, 1889, T. 4, p. 472, Figure 862.

13. Hammar, J. A.: 1915, loc. cit.

faces are markedly convex, bulging into the pleural cavities. He states that in the course of postfetal life the form of the organ changes into a less wide and more lengthy one, but that he is unable to say at which time the relations of the thymus in the new-born are replaced by those prevailing in the older individuals. However, he makes the suggestion that this change may take place in some definite relation to breathing. Hammar's illustrations of a dissection of the thorax of the new-born child clearly show the decidedly broad type of thymus; and the anterior borders of the lungs are sharp and do not overlap the anterior aspect of the thymus. Since the margins of the lungs in Hammar's figures are so sharp, and since there is no molding of the thymus by the lungs, it is most probable that these individuals must have been stillborn. This conclusion is further strengthened by the examination of Hammar's cross section figures of the new-born child. In these the thymus is extremely broad, and its lateral surfaces bulge into the medial surfaces of the lungs which do not overlap the anterior surface of the thymus in the slightest degree. His picture of the thymus shows it to be of the distinctly broad type. Apparently, the material used by Hammar was stillborn.

Since the completion of the work on which this paper is based there has come to hand a recent issue of the Anatomische Hefte containing an article by Graper.[14] In his discussion of the thymus he draws some conclusions which are similar, in part, to some of the results obtained by me. Graper states that the form of the thymus is altered during the first few breaths. It is compressed laterally by the expanding lungs and as a result its sagittal diameter is increased. He finds that after compression the thymus is triangular in cross section with the base of the triangle posterior, and that the elevation of the anterior chest wall during the establishment of respiration creates a space into which the thymus accommodates itself. His conclusions are based on a study of over fifty preserved cadavers but are not checked by necropsy findings.

The descriptions and figures in the literature of thymus glands of children later than the neonatal period [10] (especially in early childhood) are all of the elongate type and show marked molding by the lungs. Sobotta, in Bardeleben,[10] has a picture of the thymus of a 2 year old child. Even though it is not in situ, it is seen to be elongate and molded. He also presents an anterior dissection of a 14 year old girl. The thymus is markedly elongate and molded. Piersol [10] illustrates a cross section of the thorax of a child about one year old. The thymus is overlapped by the right lung and thus molded. This is also an elongate

14. Graper, L.: Die anatomische Veränderung kurz nach der Geburt. Anatomische Hefte **59**:45, 1920.

thymus; however, I have seen corresponding thymus glands in much younger individuals. Olivier [10] presents a drawing of a dissection of a one month old infant's thorax. He states that it shows the normal type of thymus. It is a bilobed organ whose lobes are widely separated and relatively very small. It is similar to thymus glands which I find in much older children. Since Olivier states that only two of his dissections were of infants, it seems probable that he had in this case the thymus of an infant in which a marked involution of the thymus had occurred.

4. RÉSUMÉ

1. The lobation of the thymus is determined early in fetal life and the establishment of respiration obviously has no effect on it.

2. The thymus in the late fetus and in the new-born is predominantly of the cervicothoracic type, i.e., its position is intermediate between the cervical location in the embryo and the thoracic location of the older infant, child and adolescent.

3. The thymus in the late fetus and stillborn child has a typical form and quite constant relations. Its lateral surfaces are convex and bulge against the medial surfaces of the lungs. The lungs very rarely extend at all on its anterior surface, and the thymus very rarely extends at all on the anterior surface of the right ventricle of the heart.

4. The thymus in liveborn infants has typical form and relations which are similar to those found in young children. It is elongated and molded so that its anterior, lateral and posterior surfaces bear the impress of all the organs with which it is in contact. Its lateral surfaces usually show marked convexities which are occupied by the lungs which pass over the anterior surface of this organ. Unlike the fetal thymus, it usually extends more inferiorly passing over the right ventricle.

5. The change from the broad or fetal type of thymus to the elongated and molded type found in the liveborn and in the young infant bears a direct relation to the establishment of respiration, and is dependent on the expansion of the lungs. The organ is compressed from side to side by the medial surfaces of the expanding lungs. It is compressed anteroposteriorly by the anterior borders of the lungs which become much thickened early in the establishment of respiration as they gradually overlap the thymus.

6. In some cases the thymic substance may extend posteriorly at birth to such an extent that the structures situated there are compressed by it. This may be due either to an unusually large thymus or to a very narrow superior thoracic aperture which will not allow the thymus to protrude into the cervical region as it is compressed by the expanding lungs.

7. The descriptions and illustrations in the literature of the thymus in the new-born child show great confusion. They include both the fetal (broad) and infantile (narrow or elongate) types and the distinction between the two has evidently passed unrecognized. The type of thymus which is the more frequently described as characteristic of the new-born and the infant is the one which the preceding data indicate is usual for the fetus and stillborn as contrasted with the living infant.

LESIONS OF THE CORPUS STRIATUM IN CHILDHOOD, WITH REPORT OF CLINICAL CASES ILLUSTRATING VARIOUS SYNDROMES*

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Every physician who deals with any considerable number of children with paralysis of cerebral origin is impressed by the fact that the motor disturbances vary enormously in type. Most common, perhaps, is the conventional spastic type, either hemiplegic or paraplegic, with scissors gait, contractures and increased reflexes. Others show bizarre abnormalities of motion, speech defect and changes of muscle tone, without great variations in reflexes. Mental defectiveness of any degree may accompany the motor manifestations.

Pathologically, a wide variety of lesions have been described, and the searcher in the literature is left with a confused idea that so many causes may produce cerebral palsy, that it is useless to try to localize lesions accurately.

As a result children with cerebral palsies have, to a large extent, been grouped as essentially hopeless, except as tenotomies or nerve section might relieve disabling spasticity or contracture. Classification has been distinctly unsatisfactory, and a considerable array of names, mostly descriptive of symptoms, has added to the confusion.

This paper is written to put before pediatricians certain facts, recently established by workers in several countries, and to show that lesions of the corpus striatum can logically account for the symptoms of a group of children with motor disabilities, who show disturbance of associated movements, variations in muscle tone and defects of speech. I believe that accurate prognosis and logical therapeutic efforts will be assisted by the separation of these cases from other cerebral palsies.

Six cases are presented to show some of the different syndromes resulting from lesions of the corpus striatum in childhood. Of course, it is obvious enough that, without necropsies, such cases are not conclusive, but a study of the literature, and frequent consultation with others, convinces me that there are sound reasons for classifying the cases definitely.

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* Received for publication May 9, 1921.

* From the Children's Hospital, Boston, and The Department of Neurology, Harvard Medical School.

HISTORICAL

During the past ten years several researches of fundamental importance, reinforced by numerous reports of carefully studied clinical cases, have done much to clarify our conception of disturbances of motility.

In 1895, Anton [1] described a case of bilateral athetosis with lesions largely confined to the putamen of the lenticular nucleus. Little importance was attached to Anton's paper until 1911, when Cecile Vogt,[2] working with Oppenheim [3] and others,[4] confirmed Anton's work and established the fact that lenticular lesions were frequently found in necropsies on cases showing bilateral athetosis. In 1911, Wilson [5] published a classical paper on lenticular degeneration with cirrhosis of the liver. Five years later Hunt [6] described cases of juvenile paralysis agitans with lesions of the lenticular nuclei. From 1908 to the present time various papers have been published tending to show that dystonia deformans, a disease characterized by variations of muscle tone leading to extraordinary deformities, and athetosis, is also due to lenticular disease. Various contributions have been published on other diseases, such as Huntington's chorea and paralysis agitans, which add weight to the conviction that the corpus striatum is a fundamental factor in the control of motility.

ANATOMIC CONSIDERATIONS

The gross anatomy of the corpus striatum is well known. Under this term I include the lenticular and the caudate nuclei. The caudate nucleus lies in the floor of the lateral ventricle. In part, it is continuous with the lenticular nucleus and in part it is separated from it by the fibers of the internal capsule. The lenticular nucleus, almost entirely surrounded by medullated fiber tracts, is divided into an inner portion, the globus pallidus, and an outer portion, the putamen. It is the putamen which joins, in front, the caudate nucleus. Figures 1, 2, and 3 illustrate the relations of the corpus striatum.

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1. Anton, G.: Ueber die Beiteiligung der grossen basalen Gehirn-ganglien bei Bewegungsstörungen und insbesondere bei Chorea. Jahrb. f. Psychiat. **14**:141, 1895.

2. Vogt, C.: Syndrome du corps strié. J. f. Psychiat. u. Neurol. **18**:478, 1911.

3. Vogt, C. and Oppenheim, H.: Wesen und Localization der kongenitalen und infantilen Pseudobulbarparalyse. J. f. Psychiat. u. Neurol. **18**:293, 1911.

4. Freund, C. S. and Vogt, C.: Etat Marbré, etc. J. f. Psychiat. u. Neurol. **18**:489, 1911.

5. Wilson, S. A. K.: Progressive Lenticular Degeneration with Cirrhosis of Liver, etc., Brain **34**:295, 1911.

6. Hunt, J. R.: Progressive Atrophy of the Globus Pallidus, Brain **40**:58, 1917.

Wilson [7] demonstrated, in the ape, the fiber connections of the corpus striatum. He showed that the caudate and the putamen are intimately bound to each other and to the globus pallidus. No fibers cross between the corpora striata of opposite sides. No fibers pass to the cortex or to the pyramidal tracts. Fibers from the corpus striatum pass to the thalamus and to certain subthalamic structures, notably to the red nucleus. Tracts, or fibers, from the thalamus and subthalamic nuclei enter the corpus striatum. Connection with the cord is assumed through synapses in the red nuclei and the rubrospinal tracts.

Microscopically two main types of cells are found: (1) Large cells, of the type elsewhere associated with motor activity. These are chiefly

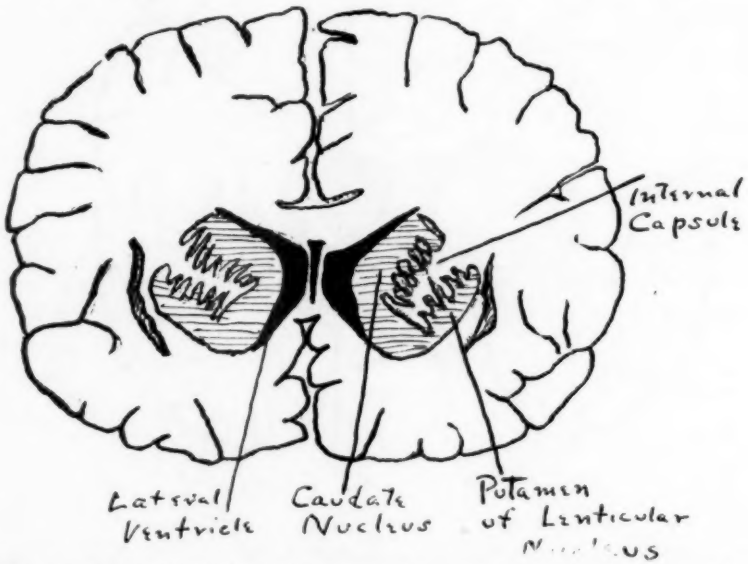

Fig. 1.—Frontal section of brain through anterior part of corpus striatum, showing putamen and caudate, partly separated by internal capsule.

found in the globus pallidus, and as they are phylogenetically and ontogenetically older than the other cells of the corpus striatum, they are called, collectively, the paleostriatum. Hunt proposes that these large cells be known as the pallidal system, including those scattered through the putamen and the caudate. (2) Small cells, younger in development, form the bulk of the cellular elements in the putamen and caudate. This group is known as the neostriatum.

PHYSIOLOGIC CONSIDERATIONS

In cats, section of the brain just above the red nuclei produces the decerebrate rigidity of Sherrington. The animal remains rigid, with

7. Wilson, S. A. K.: Experimental Research into the Anatomy and Physiology of the Corpus Striatum, Brain **36**:427, 1914.

extension of the legs, stiffness of the back and arching of the neck and tail. If by a more anterior section, the basal ganglia are left, but the cortex removed, progressive movements are possible. The suggestion is obvious that the progressive associated movements are controlled in some way by the basal ganglia. As the thalamus is apparently purely sensory in function, it is reasonable to suppose that the corpus striatum is the responsible factor.

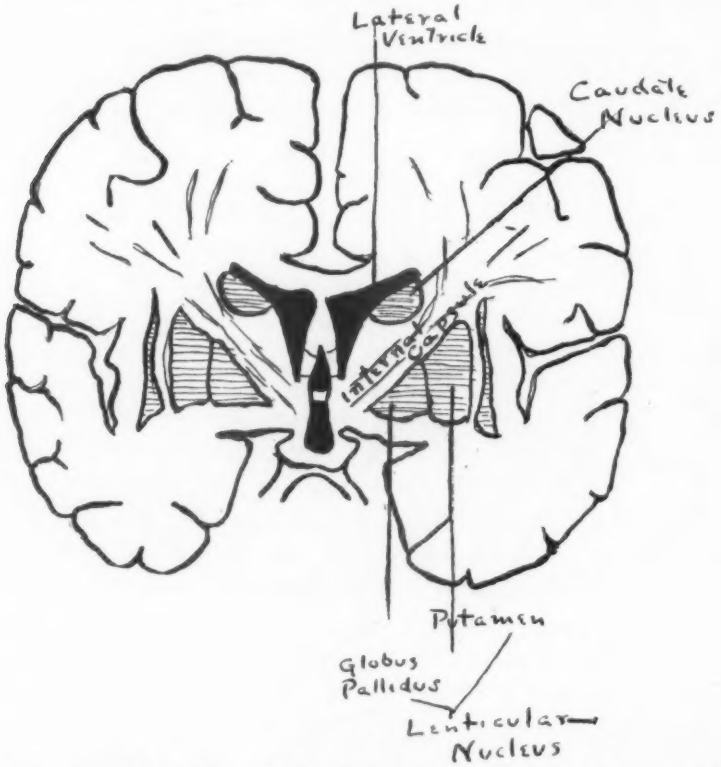

Fig. 2.—Frontal section of brain through the foramen of Munro, showing capsule separating the caudate from the lenticular nucleus which now includes globus pallidus.

Wilson,[7] working with Horsley, attempted to reproduce clinical syndromes by destruction of the corpus striatum in apes. Though his work was fruitful from the point of view of fiber tract study, he failed to produce definite motor disturbances. It is particularly noteworthy, that he was unable to produce motor activity in any way comparable with the motor manifestations obtained by cortical stimulation.

PATHOLOGIC AND CLINICAL CONSIDERATIONS

Anatomically, we have seen that the corpus striatum of each hemisphere consists of a small celled neostriatum closely connected with a

group of cells larger in size and motor in type, called the paleostriatum. The paleostriatum is independent of cortex and pyramidal tracts, but closely linked by afferent fibers with the thalamus and associated nuclei and by efferent fibers with subthalamic groups of cells, of which the red nucleus seems the most important.

Physiologically, meager evidence of control of associated movements is alone available.

Fortunately, sharply localized lesions of the corpus striatum, associated with striking clinical syndromes, clear up many points, and allow us to get a fairly good working knowledge of the function of the lenticular and caudate nuclei.

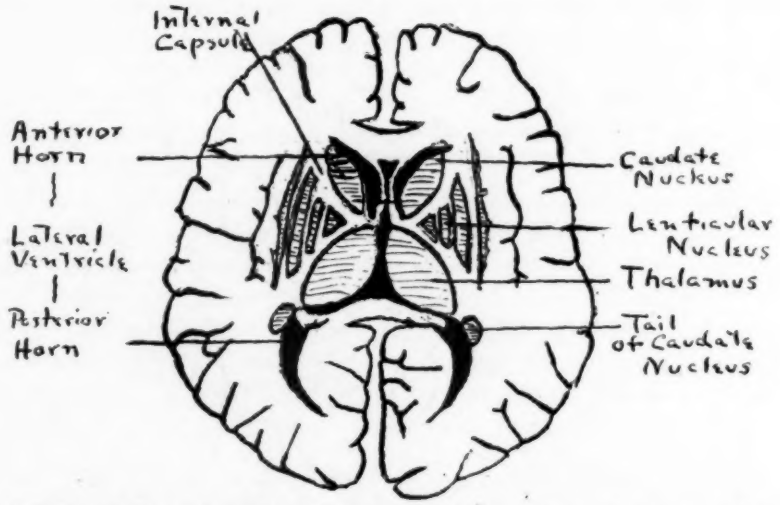

Fig. 3.—Horizontal section of brain showing relations of corpus striatum, ventricles and internal capsule.

For purposes of understanding the various types of disorder to be described, it is necessary to straighten out the nomenclature. Many authors refer to the lenticular nucleus as the corpus striatum, neglecting entirely the caudate. For practical purposes, the so-called lenticular lesions will be assumed to cover lesions of the entire corpus striatum, except as they are limited to the paleostriatum or the neostriatum. This, perhaps, unjustified assumption is made in order to avoid constant explanation. Every histologic and anatomic consideration makes it probable that the caudate and the putamen are essentially a unit, quite artificially set apart by the internal capsule.

The following syndromes are fairly well defined and more or less thoroughly established pathologically and help to a clear conception of the rôle of the corpus striatum:

1. Double athetosis, as described by Anton and Vogt. Here we have choreiform or athetoid movements, especially apparent on intention, with frequent difficulty in speech and swallowing. Associated movements are disturbed, but rigidity is relatively slight. Ocular movements are normal and reflexes are not disturbed. Clinically, this picture suggests a disorder of control rather than a paralysis. Pathologically, the small neostriatal cells are chiefly affected. Vogt has described the lesion as état marbré. The streaks of white seen in the sections are apparently due to myelinated fibers, replacing the degenerated cellular elements.

The course of this disease is peculiar. Starting at birth, or in early childhood, there is little progression and the condition is consistent with a long and mentally normal life. Occasional occurrence of two cases in one family is noted.

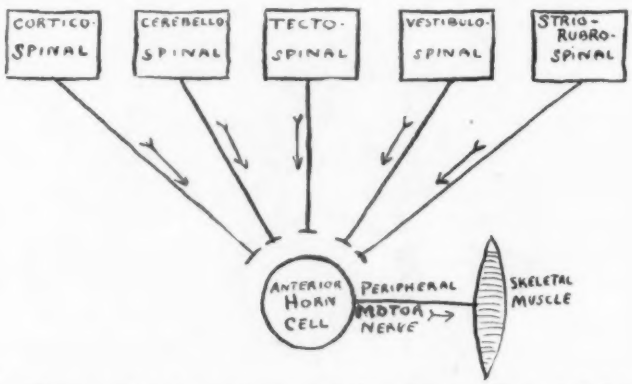

Fig. 4.—Diagram showing main tracts influencing motility of skeletal muscle. For clearness cerebellar impulses are grouped, though, actually, they are exerted through various paths.

2. Juvenile paralysis agitans, as described by Hunt, consists of extreme rigidity with tremor, without choreiform or athetoid movements. It is progressive and leads to helplessness and spechlessness, without, necessarily, mental impairment. The reflexes, except as masked by rigidity, are normal.

Pathologically, the large motor cells of the paleostriatum are involved. Hunt regards the disease as essentially a paralysis of associated movement.

3. Rigidity, tremor and, occasionally, choreiform or tonic spasms occur in the progressive lenticular degeneration with cirrhosis of the liver, described by Wilson. In these cases both neostriatum and paleostriatum are involved. Hunt regards Wilson's syndrome as essentially rigidity plus chorea, but it is obvious that certain of Wilson's cases showed only tremor and rigidity. Steady progressive disability

leads to death in a few years. In Wilson's cases a remarkable family tendency was observed. No clear hereditary factors have been worked out.

4. Dystonia lenticularis; a disease characterized by a wide variety of athetoid movements, made even more bizarre by differences in tone between various muscle groups. This tone variation leads to more or less permanent deformities of which the characteristic dromedary back, shown in photographs of Case 1, is the most typical. Regarded by its first describers as a neurosis it was not until Thomalla's [8] paper in 1918 that careful pathologic studies showed changes in the putamen of the lenticular nucleus and liver changes, thus establishing, for the present, its status as a disease of the lenticular region. Taylor [9] summarizes recent literature and reiterates Thomalla's argument that intermediate forms, linking together the various syndromes, occur.

These four syndromes are associated with clean cut lesions of very definite type. However, anyone reading case reports is struck by the extremely atypical character of certain of the symptoms in cases where autopsy confirmed the diagnosis.

For example, Thomalla's case of dystonia showed, for a short time, the prolonged muscular contractions usually associated with Thomsen's disease (myotonia congenita), while other cases show Babinski's phenomenon, unequal reflexes, etc.

In addition to these four groups in which lesions are confined to the corpus striatum, there are many cases in which the disturbed involuntary movements, so characteristic of lenticular lesions, occur in children showing, in addition, indisputable evidence of lesions of the corticospinal neurones, that is, spasticity, exaggerated reflexes, Babinski's phenomenon or clonus. This is not unexpected if we realize the intimate relations of the internal capsule and the corpus striatum. Furthermore, it is a commonplace that the "arteries of cerebral hemorrhage" are those of lenticulostriate groups, which supply the capsules and parts of the basal ganglia. This group of cases presents, naturally, a wide variety of clinical pictures, depending on the extent of the lesions and the relative damage to capsule and nuclei. Except for Thomas's [10] cases, I have found no reference to family susceptibility. Apparently this combined involvement of the capsule and the corpus striatum can be the result of hemorrhage or of degenerative processes.

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8. Thomalla, C.: Ein Fall von Torsionsspasmus mit Sektionsbefund und seine Beziehungen zur Athétose double, Wilsonische Krankeit und Pseudosclerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **41**:311 (June) 1918.

9. Taylor, E. W.: Dystonia Lenticularis, Arch. Neurol. & Psychiat. **4**:417 (Oct.) 1920.

10. Thomas, J. J.: Chronic Progressive Lenticular Degeneration with Mental Deterioration, J. Nerv. & Ment. Dis. **47**:320 (Nov.) 1917.

From a consideration of these various facts it is possible to arrive at fairly definite conclusions.

It seems clear that the paleostriatum is the motor center for certain associated movements, which are controlled and steadied by the neostriatum. This mechanism functions without direct connection with the corticospinal neurones. This idea of an autononous motor system is carried further by Hunt [11] who has developed the hypothesis that the peripheral nervous system has one set of fibers for pyramidal impulses and another for impulses arising in the corpus striatum. He further regards it as probable that these two groups act on different elements in the muscle tissue. His work is backed up by a considerable body of clinical and physiological evidence and must be followed with the greatest interest.

The present view of motor control of other observers is based chiefly on Sherrington's [12] conception that the anterior horn cell with its axis cylinder forms the final common path over which all impulses to the muscle must pass. Figure 4 shows the chief motor tracts. The lesions of the various tracts cause specific disorders, as follows:

1. Corticospinal: Spastic paralysis with increased reflexes and Babinski's phenomenon.

2. Cerebellospinal: (Under this name are grouped all fibers acted on by cerebellar cells, though they constitute no definite single tract), ataxia, asynergia, atonia and the like.

3. Tectospinal: Disordered reflexes depending on sight and hearing.

4. Vestibulospinal: Vertigo and disturbances of balance.

5. Striorubrospinal: The results of lesions of this tract are those discussed in this paper and consist of disorders of associated movements and variations in muscle tone.

It is obvious from Figures 1, 2 and 3 that lesions of the corpus striatum may involve the corticospinal tracts leading to such combinations of athetosis and spasticity, as are frequently seen in hemiplegias due to lesions of the lenticulostriate arteries.

Hunt's conception, of course, demands two final common paths, one of which is acted on by the first four tracts, while the second receives its chief impulses from the corpus striatum alone.

Probably, we cannot obtain typical corticospinal spasticity as a result of cerebral lesions without relatively intact striorubrospinal tract, and vice versa. This is strikingly suggested by the fact that an ordinary

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11. Hunt, J. R.: Transmission of Motor Impulses in Peripheral Nerves, Brain **41**:302, 1918.

12. Sherrington, C. S.: Integrative Action of Nervous System, New Haven, 1906.

hemiplegia, occurring in a patient with paralysis agitans, produces paralysis without tremor or spasticity on the affected side. As the pyramidal lesion clears the tremor and rigidity return.

A consideration of the various fundamental papers, with due weight given to the numerous case reports now available, leads to the question of grouping. No entirely satisfactory nomenclature is available. This phase of the question will be considered again, in connection with the case reports.

However, from the point of view of treatment, two main groups are suggested. In the first would fall Wilson's disease, dystonia lenticularis and juvenile paralysis agitans. These syndromes are, apparently, the result of symmetrical degenerative lesions; they are progressive, and offer little hope for arrest or for effective treatment. On the other hand, the cases of double athetosis, and certain cases showing a mixture of spasticity and disturbed associated movements are, as far as I have learned, usually not progressive and are reasonably hopeful. In many of these cases, it seems probable that hemorrhagic lesions are responsible. Naturally, pathologic classification is uncertain, as most of the patients are still alive.

Racial factors seem to influence the form of the disease, as the majority of cases classified as dystonia occur in Jewish children.

One very important point should be considered, and that is the proper use of the term cerebral spastic paralysis. Strictly speaking, this should include both groups, the pyramidal, and the lenticular lesions with rigidity. But it seems more reasonable to classify cases as corticospinal or pyramidal, if the lesion involves those neurones, or as lenticular or extrapyramidal, if the lenticular apparatus is responsible.

The judgment of mental status is singularly difficult. The patients are almost always restricted to a very narrow life and speech difficulties are usually marked. No doubt, many children are judged too severely and regarded improperly as idiots or imbeciles. The combination of set expression and speech defect with extreme awkwardness creates an impression of defective mentality that is hard to overcome. Anyone who has had any considerable experience in checking clinical impressions by psychological tests realizes the enormous possibility of error.

CASE REPORTS

CASE 1.—One form of the progressive type of disease. The boy suffers from tremor, hypertonicity and rigidity of muscles, without any of the ordinary signs produced by corticospinal lesions.

Clinical diagnosis.—Progressive bilateral degeneration of lenticular nuclei, of type described by Wilson, except for certain features suggestive of dystonia lenticularis.

C. F., 9 years and 9 months old, was admitted to the orthopedic wards on Aug. 3, 1918.

Family History.—Parents, healthy Irish people. One sister and one brother well. (Two years later still well, except one child "not developing mentally." I have been unable to obtain an exact report on the abnormal child.)

Previous History.—Entirely normal childhood until present illness.

Fig. 5. Case 1.—Showing "dromedary back." Exposure of 1/50 second. The lack of distinction in hands is due to tremor.

Present Illness.—Five weeks before entrance, father noticed that boy carried one shoulder forward, and a few days later he began to stand crookedly.

Physical Examination.—Not remarkable, except for the following: Speech slow, without definite scanning quality. Walking difficult and movements seemed ataxic, or at least he had difficulty in balancing. All his movements were slow and awkward. Deformities, attributed to muscle rigidity, were right torticollis, right dorsal and left lumbar scoliosis. He usually kept the right

leg bent at the hip and knee. On lying down, all these abnormalities of posture cleared up. Reflexes, extra-ocular movements and fundi were entirely normal. He was discharged at the end of two weeks with the symptomatic diagnosis of myotonia.

Clinical Course.—Jan. 19, 1921 he was readmitted for further study by request of Dr. Robert W. Lovett, to whom I am indebted for the privilege of seeing and reporting this case.

During the past two and one-half years, the boy attended school regularly and had not been regarded as an invalid at home. His school work was satisfactory and his parents saw no reason for worry.

I saw him Jan. 23, 1921. He was sitting comfortably at a table and at first glance seemed quite normal. On attracting his attention, it was clear that he understood perfectly well what went on, but his facial expression did not change at all and a rather extreme smile persisted. His lower lip trembled, and occassionally a few drops of saliva dripped over it. His speech was clear and expressed his ideas unusually well for a boy of his age. No scanning quality was observed, although at times his words came jerkily and slowly. On attempts to read aloud he had difficulty with long or unfamiliar words and their pronunciation was accompanied by coarse tremor of arms and legs.

Second Physical Examination.—This showed a boy of normal stature and development. Facial expression as described. No evidence of paralysis. Eyes entirely normal including fundi, extraocular movements and fields of vision. Tongue protruded straight with slight tremor. Lower lip almost constantly tremulous with occasional escape of saliva. Palate moved normally. The rest of the body showed general rigidity. The outlines of all muscles were clearly visible and the constant slow tremor of certain groups was very striking. The individual muscles stood out sharply and alternate contraction and relaxation was clearly seen. The rigidity was most marked in the larger muscles and the small muscles of the hand and foot seemed definitely hypotonic. His posture clearly suggested variations in tone in the great trunk and thigh muscles. On tapping the muscles, sudden appearance of localized swelling was observed. Following the rapid disappearance of this swelling a tâche cerebralé appeared. Voluntary control and accurate movements of all muscle groups were observed. The awkwardness was obviously due to rigidity, tremor or involuntary movements, rather than to any lack of pyramidal control. Sensation, both deep and superficial, was entirely undisturbed. Closing of the eyes did not increase awkwardness or tremor. The reflexes, deep and superficial were entirely normal.

The mental status of the patient, whether judged by school progress, general impression or formal test was normal. By the Stanford revision of the Binet-Simon test he graded 10 11/12 against a chronologic age of 11 4/12. His handwriting was clear, though he stated it was hard to use a light pen or pencil. With a strong pencil and by the use of considerable pressure, he managed to overcome tremor. But when he was uncertain as to exact lines, as in the Binet problem of drawing a path in a circular field, marked tremor occurred. In fact, this single test showed his condition almost perfectly. The problem, found in the Stanford test for 8 years, is to find a base ball in a circular field. The subject is asked to draw his path inside a two and one-half inch circle and to continue until the ball is found. The boy solved the problem perfectly, by starting in a spiral. He was able to keep his rings about an eight of an inch apart, but the early part of the course showed continuous tremor, while as he became certain of the correct solution he drew a heavier and steadier line. On the tests requiring accurate memory and straight lines very little tremor was observed. During the test he occasionally burst into tears, without any other evidence of real emotion or excitement.

COMMENT

Further observation of the patient was most instructive. The picture as described is one dominated by rigidity, tremor and contractures. On the next day the character of the involuntary movements had decidedly altered. He showed a surprising variety of athetoid movements and relatively little rigidity. Variations in the signs occurred almost from hour to hour. By those who saw him and were familiar with recent literature, a variety of diagnosis ~~were~~ was made. Dystonia, double athetosis and Wilson's syndrome were all given, as the dominant signs came and went. More than any other case, in my experience, this boy showed unmistakable disturbance of the corpus striatum with a shifting clinical picture. Muscle tone also varied. Usually it was decidedly less in the fingers and toes than in the larger muscle groups.

No doubt exists that this case is one of double lenticular disease. The stiff smile, the tremulous lips with occasional escape of saliva, the rigidity and tremor with athetosis, make an unmistakable picture. On the whole, it seems to fit into the same category as Wilson's cases. The posture, on the other hand, suggests dystonia. Against dystonia, in its typical form, is the absence, as a rule, of bizarre involuntary movements, and to a certain extent his Irish parentage. However, the exact classification is unnecessary as the prognosis is not altered. Treatment is discouraging, as no way of stopping the steady progress of the tremor, rigidity and athetosis is known. All that can be done is to attempt to train the boy to do things that can be carried on as long as possible. The presumption is strong that total disability will occur within a very few years.

CASE 2.—This is an example of a congenital, or birth, lesion. His history shows that at first his motor disturbance was flaccid, later of the type usually associated with corticospinal lesions, finally becoming athetoid without spasticity.

Clinical Diagnosis.—Double athetosis, probably due to double lenticular lesions, caused by birth injury or by failure of development.

M. L. the sixth child of Jewish parents, entered the medical outpatient department of the Children's Hospital, May 15, 1915, aged 1 year.

Family History.—Mother and father living and well. Three other children living and well. Two died in infancy.

Previous History.—Easy labor. Small child, said to weigh only 4 pounds at birth. There was a question as to whether he was one month premature. No asphyxia or convulsions were observed.

Present Illness.—At the end of his first year he was not walking or sitting up without support and was brought to the hospital. A careful examination showed no evidence of spasticity or definite paralysis, and a diagnosis of rickets was made. He was frequently reexamined and the diagnosis was not changed until February, 1916, when he was sent to a state school for feeble minded.

He returned to the hospital in July, 1918, on account of failure to walk. Examination on the orthopedic service showed the following condition. A boy, aged 4, obviously mentally defective, with moderate rickets. Choreiform

movements of the face, spasm of adductors of thighs and gastrocnemii. Knee jerks hyperactive, with bilateral clonus at knee and ankle. Babinski on both sides suggestive. Moderate contractures of both Achilles tendons.

A diagnosis of spastic paralysis involving both legs was made and tenotomies of Achilles tendons were done. No note of any speech defect was made.

Following recovery from his operation, he returned to the outpatient department where, by training, he was enabled to walk with support.

In July, 1920, he was sent to receive further muscle training without splints. Brief notes describe his gait as extremely unsteady, showing ataxia and incoordination.

In November, 1920, I saw him for the first time. The impression of feeblemindedness was partly confirmed by the Stanford revision of the Binet test, which gave him a mental age of 4½ years, against a chronologic age of 6½. It is to be said that the impression of greater retardation was obvious and I

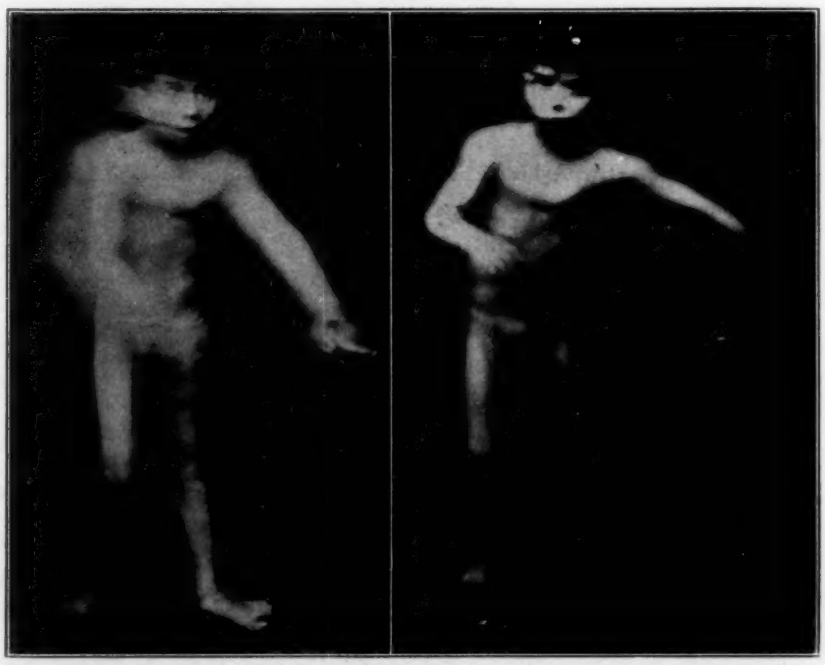

Fig. 6. Case 2.—The photographs suggest the quick, almost squirming torsion and the athetosis shown by this patient. These pictures were the clearest of a series of many taken with 1/50 second exposure.

was surprised at his ability to handle the mental test. Furthermore, I am not yet convinced that the Binet test does not underestimate the intelligence of children who are deprived of ordinary social contacts and schooling.

Physical Examination.—His general attitude is shown in Figure 6. During the entire examination, he showed a constantly changing picture of uncontrolled movements, sparing only the eyes. No cranial nerve paralyses were made out. All external eye muscles were functioning and no nystagmus was apparent. Visual fields, by rough test were normal, the tongue protruded straight, there was no palatal paralysis. His speech was extremely jerky and often almost impossible to interpret, but no aphasia existed. On attempting unfamiliar words he went through a series of contortions involving his whole body, before being able to articulate.

The examination of the skeletal muscles showed no paralysis. The muscles were stiff, without obvious differences in tone between various groups. Any abnormalities of posture were due to temporary muscular contractions rather than to permanent deformities.

His reflexes were entirely within normal limits. No Babinski or other extensor phenomena could be elicited. No clonus was observed. I particularly searched for evidence of contracture or spasm of adductors, hamstrings, or gastrocnemii and found none. Associated movements showed bizarre abnormalities. When walking, his arms moved without any relation to his legs. He was able to walk with considerable freedom, but the whole frame was involved in continuous athetosis and extreme effort was necessary to make progress. No sensory disturbances existed, as far as tests on a retarded child could be considered conclusive.

COMMENT

In babyhood this boy was regarded as a rachitic idiot. Following a two year stay in an institution for feeble minded, he showed conclusive signs of pyramidal tract involvement; spasticity, clonus and contractures, with some involuntary movements of the face, and was operated on at four years. At 6½ years he showns no signs of pyramidal tract involvement, but a clean cut picture of the type associated with lesions of the corpus striatum.

It seems reasonable to suppose that the pathologic processes in the corpus striatum involved, at one stage, the pyramidal tracts, by pressure. This would correpond with one case reported by Vogt, who found evidence of pyramidal tract pressure, manifested by apparent enlargement of the internal capsule, due to spreading of the fibers. Furthermore it is interesting to note that, in Cases 4 and 5 and in those reported by Thomas,[12] the pyramidal tracts were clearly involved in lesions clinically, primarily localized in the corpus striatum.

Another interesting feature was the error in judgment made in estimating his mentality. The impression of idiocy was far from confirmed by the result of formal testing, which showed a much higher level of intelligence than the appearance of the child suggested.

CASE 3.—This case is reported in order to show a type of cerebral palsy, without spasticity, which, I believe, is due to pure lesions of the corpus striatum. It also shows slow improvement under treatment.

P. S., aged 4½ years, was seen in December, 1920, in consultation. She is the only child of healthy parents. A few hours before her birth her mother had a rather troublesome uterine hemorrhage. Otherwise nothing to excite notice occurred until the latter part of her first year. At that time it was observed that she failed to sit up.

She never developed control over her muscles, or learned to sit alone or to walk. No systematic attempt at muscle training had been made. She learned to talk at about the usual time, but speech had always been difficult to understand. As far as the parents or the family physician know, no diagnosis beyond "cerebral disease" had ever been made by any of the various consultants who had seen the child.

Physical Examination.—This showed an extremely bright attractive child smiling cheerily. However, the impression of vivacity rather diminished

during the course of examination as the smile persisted throughout. Athetosis was marked, except for the face. Particularly when trying to speak, movements were very lively. The eyes showed no pupillary abnormalities. The extra-ocular movements were normal; there was no nystagmus and rough tests showed no limitation of visual fields. The other cranial nerves showed no evidence of involvement. The tongue protruded straight, without tremor. The mouth was held open, without evidence of nasal obstruction, or escape of saliva. A very definite fixed smile was present at all times. Dysarthria was marked, though practically all words were intelligible. No dysphagia.

The disturbances of the motor control of the trunk and limbs were very marked. Athetosis and disturbances of associated movements were particularly striking. It was impossible to close one hand, for example, and hold the other extended. Attempts at walking were grotesquely awkward, until a definite slow rhythm was adopted and then she managed fairly well, with support. Her muscles were all moderately rigid, though no spasm or contracture existed. Furthermore all muscles were well developed. No definite variations in tone were made out. Knee jerks, ankle jerks, the deep reflexes of the arm and the superficial reflexes of the abdomen were all normal. No Babinski or Oppenheim could be elicited. Sensation was normal to touch and pain and, as far as could be judged, muscle sense was not impaired. No increase of unsteadiness was observed when the child closed her eyes. Voluntary movements of all muscles were possible, and except as rigidity and involuntary motions interfered, were accurate.

No formal mental test seemed worth while, as the complete isolation of the child's life, her inability to handle concrete material and her speech defect made judgment by test practically worthless. However, she very certainly was not seriously retarded. Naturally her parents and relatives had indulged every known wish, in spite of this she was tractable in most things and very responsive and affectionate.

Under carefully supervised muscle training she has gained appreciably in control in the course of four months.

COMMENT

The diagnosis here is hardly in doubt. The congenital nature of the disease, its apparently nonprogressive character, the facial expression, the normal extra-ocular movements, the normal reflexes and the generalized disturbance of associated movement all point conclusively to double lenticular lesions. The presumption is that the lesion is that described by Cecile Vogt as état marbré of the lenticular nucleus involving, chiefly, the cells of the neostriatum.

The treatment followed is based, largely, on theoretic grounds. In a child of normal mentality a condition, which is presumably not progressive, disturbs the control of involuntary movements. The cortico-spinal neurons are apparently intact, as is muscle sense. I do not see why suitable muscle training should not develop a reasonably effective motor system. Of course, rigidity and involuntary movements will probably persist. In any case, the thorough trial of this method offers a promising field.

In Case 2 such a method, with a patient of inferior intelligence is resulting in a very decided improvement, even under unfavorable home conditions.

Further treatment can be carried out, which falls under the general term of mental hygiene. It is, of course, essential that the child be trained to obedience. The possibility of handling the various problems that inevitably will face her, with reasonable serenity, depends almost entirely on the intelligent supervision that she is able to have at present.

CASE 4.—A girl, aged 4½ years, showing bilateral athetosis and spasticity without demonstrable mental defect.

Clinical Diagnosis.—Bilateral lesions of corpus striatum, with involvement of internal capsules, probably due to birth hemorrhages.

Fig. 7. Case 4.—Illustrating the bright facial expression and the absence of conventional "spastic" posture or contractures.

M. B. was seen March 31, 1921, in the Nerve Outpatient Department. She is 4½ years old and is the only child of healthy parents. She was delivered, after twenty-four hours of labor, by forceps. Asphyxia was marked, and she required artificial respiration for a considerable time. No convulsions or stupor followed.

During the first year she appeared normal and began to speak at one year. At 18 months she tried to walk, without success. Since babyhood she has

apparently developed normally as far as mentality is concerned. Her speech is difficult to follow, but she uses a considerable vocabulary accurately, on the other hand, she has developed little motor control and is entirely unable to use her hands accurately or to walk.

Physical Examination.—Shows a well developed and bright child. Except for her motor system she shows no abnormality. No paralysis of cranial nerves exists. No nystagmus, no abnormality of pupils or eyegrounds. The difficulty in speech seems to be due to incoordination of the muscles, rather than to any other factor. The mouth remains open and occasionally there is escape of saliva. The arms and legs are distinctly stiff. This stiffness, which is definitely plastic in type, is more marked on the right side. Reflexes are lively, particularly on the right, where they are definitely above normal. Both plantar reflexes are extensor in type with fanning of the toes. A well sustained ankle clonus is present on the right and a few jerks can be elicited on the left.

Motor disturbances are very striking. Attempts at movement give rise to a variety of definitely athetoid movements. The usual attitude of "spastic paralysis" is conspicuously absent. She attempts to walk with her feet wide apart and every step is accompanied by all sorts of aimless movements of her arms. Indiviudal muscles can be used efficiently and easily, and it seems clear that difficulties arise only when smooth coordination of various groups is necessary.

No ataxia, disturbance of muscle sense or superficial sensory disorder can be made out.

COMMENT

This child illustrates, I believe, a rather common condition. The most reasonable explanation is that she had, at birth, hemorrhages in the region of the lenticular and caudate nuclei, involving the internal capsules. This would fit in with the very clear history of asphyxia. Her present condition is largely due, according to this conception, to destruction of the nuclei, with relatively little damage to the neighboring capsules. I believe that this case fits in between the pure lesion of the corpus striatum, of which Case 3 is an example, and the conventional spastic paralysis with adductor spasm and hamstring and Achilles contractures and so on.

The prognosis, of course, is doubtful, but I feel confident that the condition is not progressive, and that on the whole improvement is to be expected.

Treatment is as suggested for Case 3.

CASE 5.—This case is reported in order to show an atypical case with degenerative lesions and mental retardation. In this child the internal capsules as well as the nuclei were apparently involved.

G. C., 8 years old, was first admitted to medical wards of the Children's Hospital Aug. 28, 1919.

Family History.—Negative; father, mother, one brother and two sisters living and well.

Previous History.—Full term, normal delivery. Chickenpox, bronchitis and measles. Otherwise entirely uneventful story till present illness.

Present Illness.—June 15, 1919, kept in bed two weeks for "St. Vitus dance." Mother noticed senseless laughter and some deterioration of mentality. Then up and about, without full recovery of motor control, until August 24, when she was again put to bed. Admitted to hospital the next day.

During her stay in the hospital she had coarse tremor apparently of intention type, absent abdominal reflexes, ankle clonus at times on left, suggestive Babinski on left, no definite nystagmus. October 21, she was seen by Dr. E. W. Taylor who regarded her as having, probably, multiple sclerosis. She was discharged relieved Nov. 12, 1919.

From then until Jan. 2, 1920, she was followed by visitors who reported great speech difficulty and persistence of choreiform movements.

Second Examination.—On readmission she showed thickness of speech, occasional regurgitation of food through her nose and coarse tremor. Abdominal reflexes were not obtained, no clonus or Babinski were observed. No nystagmus. Discharged relieved March 28, 1920.

During the summer of 1920, she apparently recovered entirely, except that she twitched more or less when excited and was decidedly irritable.

From November, 1920, she became increasingly shaky and was admitted to the wards Dec. 4, 1920, when she showed much the same picture as on previous occasions. No nystagmus, no serious speech disturbance, sluggish abdominal reflexes, double Babinski, and clonus on left. Tremor was confined to the left hand.

Eye examination by Dr. H. W. Goodall showed congestion of both discs with decidedly defective vision.

I saw her repeatedly from January 6 to her discharge. When first seen, she smiled almost continuously with a rather vacant expression. Her movements were tremulous and at times definitely ataxic in character without accentuation on closing eyes. The eyes showed irregular up and down oscillations, but I could not determine that there was any nystagmus. No palsy of external eye muscles noted at first. Pupils equal and reacted normally. Tongue protruded straight with slight trembling. No palatal paralysis. No facial paralysis or asymmetry.

The arms were not stiff, reflexes normal. The left arm and hand were markedly tremulous with some movements suggesting athetosis. No weakness of any muscle group and firm contraction was easily maintained. Attempts to make definite coordinated movements resulted in ataxic tremulous movements. This disturbance was not increased by closing eyes and was apparently not due to impairment of muscle sense. The same phenomena in less degree were present on the right.

The legs showed bilateral ataxic movements, increased deep reflexes and, like the arms, apparently normal superficial and deep sensation. Babinski's phenomenon and clonus were present on left at first, later on both sides. Abdominal reflexes were obtained.

A Binet test showed a mental age of 6 9/12 compared with her present age of 9. This agrees with previous estimates in the hospital and with a history of rather unsatisfactory school work in the second grade.

Comment.—This combination of spasticity, involuntary movements of mixed tremulous and choreiform type with mental retardation suggested the atypical lenticular degeneration described by Thomas.[11] Dr. Thomas was good enough to see this patient. His examination disclosed, in addition to the previously described signs, a weakness of the right internal rectus with resultant diplopia. He agreed that the lesions were to be placed in both lenticular nuclei, with involvement of the pyramidal tracts.

This case does not fit into any definite group but the evidence is strong that both lenticular nuclei are involved. The remission suggests the possibility of the lesions being of the type of multiple sclerosis.

Against the ordinary type of multiple sclerosis is the repeated presence of abdominal reflexes, the absence of typical scanning speech and of typical nystagmus. Furthermore, no signs pointing to lesions elsewhere were obtained.

Chorea, in my opinion is unlikely for the following reasons. First, the prolonged course, second, the signs of definite pyramidal tract involvement and third, the ability to maintain a steady muscular contraction. Furthermore mental retardation is unusual in chorea, while it is common in lenticular degeneration.

I wish to thank Dr. John Lovett Morse for permission to study and report this puzzling case.

CASE 6.—This Jewish child, aged 7, with vague motor disturbance is presented, because he shows signs suggesting a mild involvement of the corpus striatum.

A tentative clinical diagnosis of lenticular degeneration was made.

J. D., 6 years and 10 months old, was admitted to Dr. J. L. Morse's service at the Children's Hospital Feb. 2, 1921. I am indebted to Dr. Morse for permission to see this case and report it.

Family History.—Negative. Both parents and two other children are well.

Previous History.—He was born at full term. Instruments were used and he had a bilateral cervical swelling, regarded by his physician as haemotomata. No asphyxia or convulsions occurred.

Present Illness.—The symptoms reasonably associated with his present condition were, first, a difficulty in getting his words out, without obvious lack of clear articulation. This speech defect existed from very early childhood and was increased following a tonsil operation in August 1920. Second, a motor disturbance, which was first noticed one year before entrance. At that time he ran sideways and shook his head, without reason. Vaguely described squirming movements followed and have persisted. No special difficulty had been observed in handling objects. His parents regarded him as normal mentally, but interested neighbors, and finally the school doctor, told the parents he was backward and nervous and suggested sending him to the hospital for diagnosis.

Physical Examination.—A well developed and nourished child lay quietly in bed. The expression was quite abnormal. The eyes were alert and gave the impression of mental activity. The lower part of the face was almost entirely immobile. The mouth was not kept open. The impassive face, added to his speech defect, created an appearance of feeble mindedness.

No abnormality of eyesight, eye movements, or eye grounds was observed. No signs pointed to involvement of any cranial nerves.

The speech defect struck me as divisable into two parts, first a distinctly scanning rhythm with occasional jerky articulation, second clumsy phonation, which I felt could be explained by a considerable tear of the soft palate, apparently resulting from the tonsil operation.

The muscle of the trunk and limbs shared in curiously vague, rather slow involuntary movements. His posture was not normal as his back was perfectly straight, without any lumbar curve. No definite changes of tone were made out. On walking he showed no tremor of marked unsteadiness, but there was no smooth coordination of arms and legs, in fact sometimes one arm would hang motionless, while the other moved about without the slightest relation to the walking rhythm.

Careful sensory examination showed no change in deep or superficial sensation.

Reflexes were normal, except that the left ankle jerk was decidedly lively and, at times two or three clonic jerks could be elicited. No Babinski was found. No paralysis existed.

Mental tests showed that the first impression of feeble mindedness was not justified. He had a mental age of 6 9/12 compared with a chronological age of 6 10/12. The rest of the physical was negative except for a heart murmur regarded by Dr. Morse as congenital, probably due to an abnormal interventricular septum. The liver extended from the fifth rib to the costal margin.

Comment.—I realize that this case is extremely vague and I quite agree with Dr. Morse in regarding the picture as too indefinite for positive diagnosis. The suggestive things, to my mind, are the following. A boy of 6, with a definite speech abnormality develops involuntary movements which persist for a year. Further, his face is so lacking in expression that many people, including physicians, have called him feeble minded. His posture is abnormal. The atypical ankle clonus on one side suggests pyramidal tract involvement.

These various facts strongly suggest the probability of a lenticular lesion, either early or slight, and can be explained in no other way that seems satisfactory. Obviously he has "chorea" of an atypical sort. Also he may be simply "nervous," but nervousness lasting a year with entire lack of facial expression is in my experience, unusual.

This case again shows the danger and injustice of judging the mentality of these children without careful investigation.

CONCLUSIONS

A number of syndromes characterized by disturbances of associated movements, variations in muscle tone, and speech defects are definitely associated with sharply localized lesions of the corpus striatum. They are easily distinguished, in typical cases, from spastic pyramidal tract syndromes and from the ordinary chorea. In atypical cases confusion necessarily arises and careful sorting out of signs is essential. I believe that a critical reexamination of children showing involuntary movements over a period of months or years, will reveal unsuspected cases. Moreover, the cases of this short series demonstrate the dangers of relying on casual impressions in judging mental status, when speech defects and motor disorders complicate the picture.

Finally, it seems reasonable to consider, whether the recent advances in knowledge of disorders of the motor apparatus do not demand a more exact nomenclature for paralyses of cerebral origin.

From every point of view, the study of cases of the type here described is well worth while. The present classification is purely tentative and, as Taylor points out, is almost certainly too rigid. Pathological studies have been very few and aetiological data are extremely scanty.

My recent experience with the syndromes shows fairly conclusively that such disorders cannot be considered rarities, and also demonstrates that general attention has not been called to this group.

Naturally, no claim is made that all cases like those reported are due to corpus striatum lesions alone. Abundant evidence shows that various other lesions may obscure and complicate the picture, and it is entirely likely that further study may modify the rather dogmatic and perhaps inaccurate views that are here set forth.[13]

I wish to express my gratitude to Miss Mary Trainor whose long experience as chief of the group of workers in the Nerve Outpatient Department has enabled her to advise and carry out therapeutic exercises in some of these cases.

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13. For a full bibliography reference to Wilson's, Hunt's and Taylor's papers should be made. The following references also bear on this subject:

Cadwallader, W. B.: Pseudosclerosis, etc., Am. J. M. Sc. **150**:556 (Oct.) 1915.

De Castro, A.: Des mouvements associés dans l'athetose, Rev. neurol. **24**:368 (Oct. 15) 1912.

Frauenthal H. W. and Rosenheck, C.: Dystonia Deformans (Case report) J. Nerv. & Ment. Dis. **52**:134 (Aug.) 1920.

Gordon, A.: Extrapyramidal Hemiplegia, J. Nerv. & Ment. Dis. **42**:157 (March) 1915.

Hunt, J. R.: Torsion Spasm (Dystonia Deformans) J. A. M. A. **67**:1430 (Nov. 11) 1916.

Marie, P. and Lhermitte, J.: Les lesions de la choree chronique progressive. Ann. de med. **1**:18, 1914.

Rhein, J. H. W.: Extrapyramidal Motor Disturbances, J. Nerv. & Ment. Dis. **42**:802 (Dec.) 1915.

Spiller, W. G.: Family form of Pseudosclerosis, etc., J. Nerv. & Ment. Dis. **43**:23 (Jan.) 1916.

Stern, G.: Zum Krankheitsgilde der "Athétose double" Monatschr, f. Kinderh. **19**:404 (Feb.) 1921.

Strumpell, A.: Wilsonische Krankheit, etc., Deutsch. Ztschr. f. Nervenh. **54**:207 (Dec. 3) 1915.

A FURTHER CONTRIBUTION TO THE STUDY OF PYLORIC STENOSIS*

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The treatment of pyloric stenosis is a topic which is still very much under discussion. This is mainly due to the fact that some clinicians advocate immediate operation while others get excellent results in many cases without such a radical procedure. Good results are often obtained without surgery because the spasm frequently relaxes when certain dietary measures are instituted. Operation, soon after the diagnosis is made, doubtless subjects many infants to unnecessary operation. On the other hand, persistence in unsuccessful feeding may increase the surgical risk.

The statement occasionally made by some pediatricians that the diagnosis of pyloric stenosis is synonymous with indication for operation is not in accord with the opinion held by the foremost surgeons in this field. Thus Downes,[1] points out very clearly that medical treatment is justifiable for a period of from seven to ten days, provided the patient does not lose too much weight (20 per cent. of the birth weight is the maximum weight loss he allows). Of the 163 cases of pyloric stenosis seen by Strauss [2] only 107 patients (65 per cent.) were operated on. He treated the remaining fifty-six medically. He says: "Not a single one of the medically treated cases returned for operation."

Most workers agree that the Fredet [3]-Rammstedt [4] operation, or a modification, is the best surgical procedure in those cases that fail to yield to proper medical treatment. It is true that some surgeons recommend immediate operative interference as soon as the symptoms of pyloric stenosis become manifest. Thus it has happened that on operation no tumor was found.[5] The abdomen was closed without further interference. Such a procedure would be perfectly legitimate if it had been shown that nonoperative treatment could only be successful in a small number of cases. But such is not the case. Besides the results

* Received for publication May 7, 1921.
* From the Pediatric Department of the Evanston Hospital.

1. Downes: J. A. M. A. **75**:228 (July 24) 1920.
2. Strauss: J. A. M. A. **75**:232 (July 24) 1920.
3. Fredet: (Dufour and Fredet), Rev. de chir. **37**:208, 1908.
4. Rammstedt: Med. Klin. **8**:1702, 1912.
5. I do not wish to discuss here the appearance and disappearance of tumors which have been observed at the time of laparotomy.

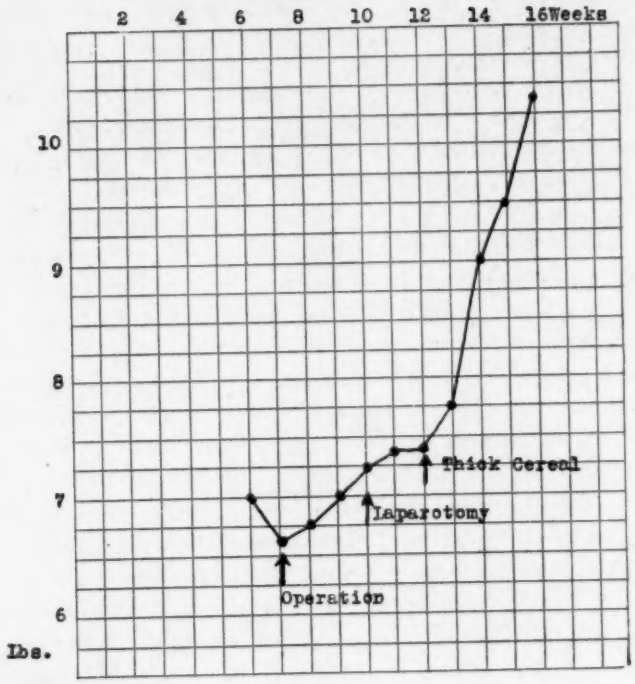

Figure 1.

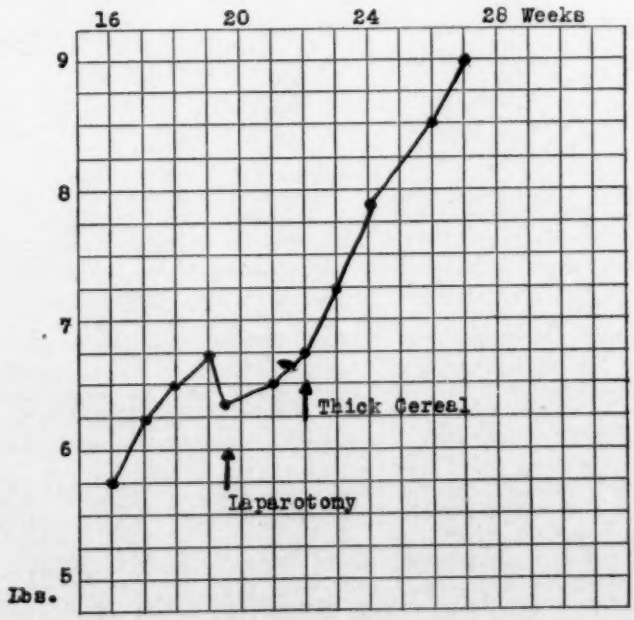

Figure 2

of Strauss, those of Heubner,[6] Ibrahim,[7] Porter,[8] Sedgwick,[9] and among others my own lend very strong support to the statement of Downes in regard to the justification of medical treatment. Indeed, it would, perhaps, be more correct to say that, as long as the patient is doing fairly well an operation is only justifiable when medical treatment has proved of no avail. An experienced surgeon can do this operation with minimal risk. On the other hand, when done by one of insufficient experience, the mortality may be very high, even when the surgical risk was very small. I speak here from experience.

That nearly moribund cases are a bad risk for the surgeon as well as for the internist is self-evident. Of the 175 patients operated on by Downes thirty died. Eighteen died from collapse shortly following operation—all were in extremely poor condition. Four others had intestinal complications, five developed peritonitis, and the remaining three died of hemorrhage. Twenty-two of his patients continued to vomit in moderate degree, and in sixteen others the vomiting occurred in large amounts. Various surgeons warn of the danger of incising the duodenum with a resulting peritonitis. Lewis [10] cautions that opening of the incision has occurred not infrequently when made in the linea alba. Of the twenty-two patients operated on by Hill,[11] two had to have the abdomen reopened. In one of the cases the opening was inadequate, in the other, the wound broke open on the sixth day and on re-operating adhesions were found.

Two cases with severe symptoms of postoperative obstruction in which the Fredet-Rammstedt operation had been performed by skilled surgeons are of interest; so is a case in which the operation was inadequate as all the symptoms of pyloric stenosis persisted for weeks until thick cereal feedings were substituted for the breast milk feedings.

REPORT OF CASES

CASE 1.—(31) Alene T., was born Aug. 29, 1920, weighing 7 pounds, 12 ounces. When seen the first time at the age of 6 weeks the vomitus contained blood. On trying thick cereal feedings for a week, the vomited material contained more blood. The Strauss modification of the Rammstedt operation was performed. The result was gratifying, the vomiting ceased and the child gained in weight on breast milk feedings. On the sixth day, the little patient developed a cold with frequent coughing and sneezing. On the eighth day the nurse noticed that the stitches had sloughed and that the wound had partly opened with a partial evisceration. The intestines were immediately replaced and the wound closed. There was no rise in temperature, and after a few

6 Heubner: Lehrbuch der Kinderheilkunde, Ed. 3, Vol. 1, p. 218.
7. Ibrahim: Die Angeborene Pylorusstenose, Berlin, 1905. Ergebnisse d. Inn. Med. and Kinderh. **1**:208, 1908.
8. Porter: Arch. Pediat. **36**:385, 1919.
9. Sedgwick: Journal Lancet **37**:437, 1917.
10. Lewis: J. A. M. A **75**:232 (July 24) 1920.
11. Hill: J. A. M. A. **75**:232 (July 24) 1920.

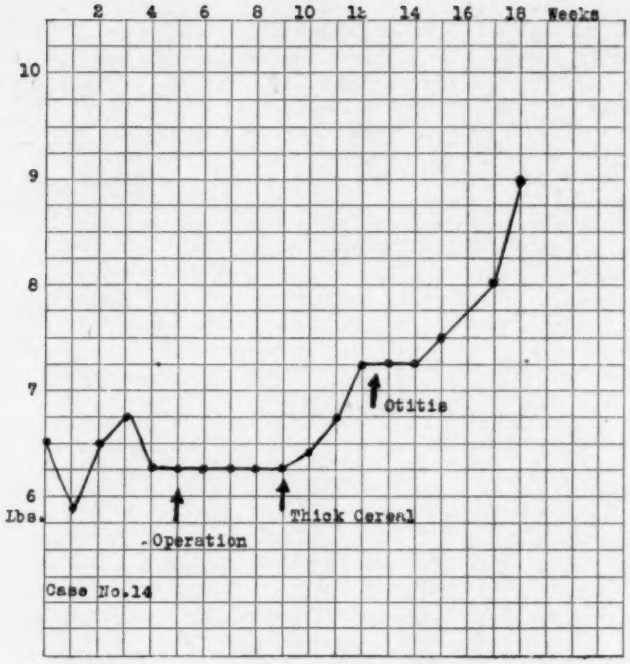

Figure 3.

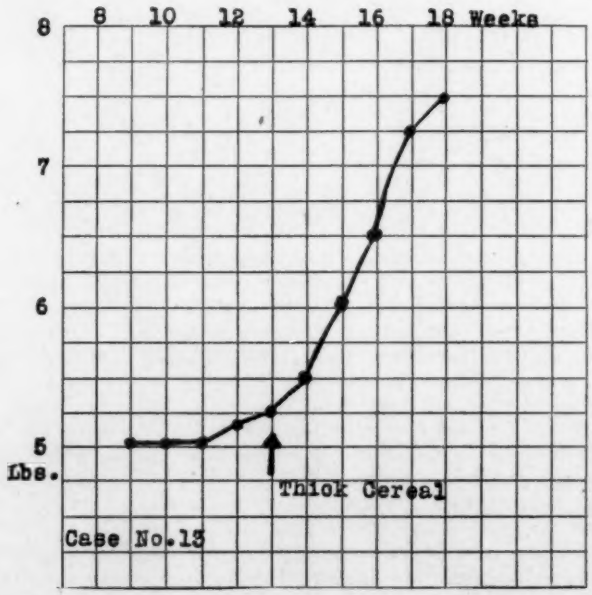

Chart 4, Case No.13, Rosie R.

Figure 4.

weeks the child was sent to the Evanston Hospital. During the following weeks, there was more or less vomiting and the gain in weight was negligible. On the twenty-first day after operation the vomiting became projectile and incessant, the child became toxic and the bowels failed to move. The abdomen was soft, although intestinal peristalsis could be seen through the thin abdominal wall. The abdomen was reopened within twenty-four hours after the onset of severe symptoms. The skin incision was made parallel and lateral to the original one. A loop of small bowel had grown firmly adherent to the parietal peritoneum along the entire incision and was removed with difficulty. Laparotomy revealed numerous adhesions and bands. These were released and due to the moribund condition of the infant about 80 c.c. of uncitrated blood was given into the sinus. Recovery was very slow during the following two weeks. As more or less vomiting continued, barley flour paste made with breast milk was started two weeks after the laparotomy. The vomiting ceased at once and the child gained 7 ounces the first week and 1 pound the following week (Fig. 1). She is now 8 months old and weighs 17 pounds.

CASE 2.—Violet S. was seen for the first time Jan. 19, 1921, at the age of 4 months, weighing 5 pounds and 12 ounces. The Rammstedt operation had been performed at the age of 6 weeks. There had been no gain in weight since the operation. The athreptic infant was getting condensed milk, had an enteritis and bronchitis with a temperature of 101 F. There was no vomiting. The child was given 50 c.c. of uncitrated blood intra-muscularly and fed breast milk. In the course of the following three weeks the infant gained 1 pound. February 7 severe vomiting, constipation and toxic symptoms rapidly developed. The abdomen was soft. Laparotomy was performed thirty-six hours after the onset of symptoms. The report of the surgeon, Dr. W. C. Danforth, follows:

> The child was extremely emaciated, the abdominal wall thin, moderately distended but without rigidity, showing very plainly distended coils of intestines. On opening the abdomen, many adhesions were present, omentum to abdominal wall at the site of the previous scar, light adhesions of coils of bowel one to another and in the ileum volvulus involving five inches of bowel twisted sharply on its mesentery. The strangulated area of bowel was very dark in color, but showed slight improvement in color on relief of the volvulus. In the mesentery thrombotic enlarged veins were seen. The intestine below the area involved in the volvulus was flattened, resembling coils of tape. As the strangulated bowel, after the application of hot laparotomy pads for a few moments, showed a slight improvement in color, and as the child's condition was desperate, it was determined to do nothing further and the abdomen was closed.
>
> The essentials of the convalescence are noted in Dr. Sauer's report. We were greatly and agreeably surprised at the recovery which the child was able to make.

The moribund infant was given 60 c.c. of uncitrated blood into the sinus. The recovery was slow during the following two weeks. February 27 the infant was given barley flour paste made as follows: Skimmed milk, 12 ounces; water, 4 ounces; barley flour, 2½ ounces; dextri-maltose, 1 ounce. Boiled one hour. Two and one-half ounces in four feedings; three ounces breast milk in three feedings. The infant gained 8 ounces in the following week, 10 ounces the week after that. She now weighs over 10 pounds (Fig. 2).

CASE 3. (14).—Nancy B., was born Dec. 15, 1918, weighing 6 pounds 10 ounces. When seen the first time (Jan. 17, 1919) the infant had a temperature of 102 F. besides manifesting the typical symptoms of stenosis. A tumor could not be palpated, and the child was having from three to four stools a day (the family physician having ordered 15 drops of milk of magnesia before each nursing). Dextrose—Ringer's solution was given by rectum and subcutaneously. A catherized specimen of urine contained much pus, albumin and hyalin casts. The temperature varied from 101-105 F. The Rammstedt operation was performed January 24. An average sized tumor was found. She received breast milk until February 22 (four weeks) without any influence on the vomiting or weight. As the bladder condition had cleared up and the temperature was normal or subnormal, it was considered safe to begin thick cereal feedings. This was done cautiously during the following week. The

food was made as follows: Cow's milk or breast milk, 12 ounces; water, 8 ounces; barley flour, 2 ounces; dextri-maltose, 1 ounce. Boiled one hour. By the end of the first week of thick cereal feeding breast milk was discontinued entirely. She made an uneventful recovery (Fig. 3).

These three cases show what complications may occur after operation, even when operation is performed by skilled surgeons. These cases fall in line with observations published by other observers.

A few remarks about operative cases may not be amiss. Fluids should frequently be given subcutaneously or by rectum before or immediately after the operation. Blood, intramuscularly or into the

Fig. 5. Case 13. Series A.—Two hours after bismuth milk feeding (Strauss position).

sinus, is of unquestionable benefit in extreme cases. Breast milk should be given whenever available. If the supply is insufficient, albumin milk may be of value. Morgan [12] and Goldbloom and Spence [13] have detailed the postoperative management of Downes' cases.

Heubner, feeding breast milk to twenty-one infants with pyloric stenosis, had a mortality of 9.5 per cent., Sedgwick, using the same method in forty-four cases, lost but one patient. Of the eighty-three cases collected from the German literature by Ibrahim, the mortality

12. Morgan: Am. J. Dis. Child. **11**:245 (March) 1916.
13. Goldbloom & Spence: Am. J. Dis. Child. **19**:263 (March) 1920.

was 22.9 per cent. Finkelstein and Meyer [14] claim that no method of feeding will stop the vomiting in pyloric stenosis. On the other hand, Birk [15] advocated the use of cornmeal gruel. In his book a weight chart shows very conclusively that the infant gained rapidly as soon as this food was substituted for breast milk. Porter, using my method of cereal feeding, got rapid cures in ten successive cases. Moll [16] reports good results with cake-flour paste.

Thick cereal feeding is not a panacea for pyloric stenosis. There are undoubtedly cases which do not respond to the treatment as

Fig. 6. Case 13. Series A.—Four hours after bismuth milk feeding (Strauss position).

expected. Sometimes this is the fault of the physician and not the patient. Several of my patients (Cases 6, 8, 18) would doubtless have made more rapid progress if the proper precautions had been taken throughout the treatment. In favorable cases, the immediate decrease or cessation of vomiting and the rapidity of weight increase is very striking (see table).

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14. Finkelstein and Meyer: Deutsch. med. Wchnschr. **45**:873 (Aug. 7) 1919.
15. Birk: (translated by Schlutz) N. Y. Rebman & Co., 1916.
16. Moll: Ztschr. f. Kinderh. **22**:147, 1919.

Success often depends on the proper preparation and administration of the thick cereal. It must be cooked thoroughly and be sufficiently thick to adhere to an inverted spoon. The influence of consistency is illustrated by the following two cases:

CASE 4 (6).—Nelson L., weight 8 pounds and 4 ounces at birth, was seen for the first time at the age of 3 months. Various pediatricians had seen him and had tried various dietary measures. A tumor was palpable. One insisted that operation was necessary. Dr. H. F. Helmholz prescribed thick cereal feedings. There was no gain in weight and the projectile vomiting continued for ten days. On visiting the home it was found that the consistency of the food was

Fig. 7. Case 13. Series A.—Four hours after bismuth milk feeding. (Nothing has left the stomach).

too thin. When this error was corrected, the vomiting immediately became less and the gain in weight was rapid. Peristaltic waves persisted for many weeks but all other symptoms of stenosis soon disappeared. The child now attends school and has never had a recurrence of symptoms. He is about 10 per cent. above the average weight for his height.

CASE 5. (16).—Thomas N., weighing 7 pounds and 14 ounces when first seen at the age of 6 weeks, presented a typical picture of stenosis. As the milk mixture the physician had ordered was considered adequate, the only change made in the diet during the first month was the addition of six tablespoonfuls of farina. This made the food sufficiently thick and the vomiting became very much less. He gained 17 ounces during the first month of this feeding.

One part of cereal to seven parts of fluid (three of milk and four of water), boiled in a covered double boiler for an hour, usually makes a cereal of proper consistency. Such a food consists of about 15 per cent. cereal. Sugar and salt may be added. Most of the cases were started on a cereal as follows, and then the proportions were changed from time to time as occasion demanded: skimmed milk, 9 ounces; water, 12 ounces; farina or rice flour, 6 teaspoonsful; dextri-maltose, 3 ounces. Boil an hour or more in a covered double boiler until thick. The consistency of the food requires careful supervision.

Fig. 8. Case 13. Series B.—Two hours after bismuth cereal feeding (Strauss position).

A satisfactory way to give the food is to have the required amount of the prepared food in a cup immersed in a shallow saucepan containing hot water. By taking a little of the warm, thick cereal on the end of a narrow tongue depressor it can very easily be placed far back into the open mouth and scraped off with another tongue depressor. Porter recommends the use of a hygeia nipple with an enlarged hole. A great deal of patience is usually required the first few days, as the young infant often keeps the thick cereal in the mouth some time before swallowing it. At first, an hour or more may be required to give a feeding of a few tablespoonsful, but this difficulty is soon overcome in most cases. Twenty-one of my patients were taken care of in the home by the mothers.

From two to six tablespoonsful of such cereal may be given six or seven times a day. When breast milk is available, one may try giving one or more tablespoonsful of the cereal before the nursing or bottle breast milk feedings. If such a régimé proves unsuccessful, four thick cereal feedings and three breast milk feedings should be tried for a few days. If this fails to stop the vomiting and loss in weight, then all feedings should consist of the thick cereal. In severe cases, the latter procedure should be instituted at once., Any available breast milk should be added to the cereal replacing the cow's milk. The child should be placed on its right side for a few hours following the feed-

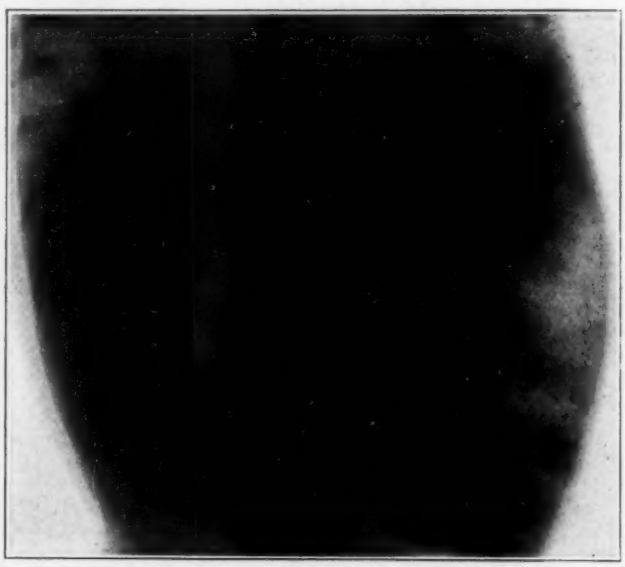

Fig. 9. Case 13. Series B.—Four hours after bismuth farina feeding (Strauss position).

ing. It must be handled very little and should rest on a medium soft pillow. In my last twenty-four cases the stomach was not washed out, in fact, very little fluid was given by mouth for the first few weeks. Water must be furnished at regular intervals, preferably by retention enema, by the Murphy drip method or by hypodermoclysis.

After thick cereal feedings have been persisted in for some time, liquid foods also pass through the pylorus. This interval varies in different cases—it usually requires at least from five to eight weeks before an appreciable amount of liquid food can be given without being vomited. The safest way to proceed when this time has apparently arrived is to substitute for one and later for several of the thick cereal feedings ordinary milk mixtures. If vomiting is not provoked in this

way the child can be put on a milk mixture without much further trouble in spite of persistent peristaltic waves and palpable tumor. During the past few years rice flour and barley flour have been used in place of or in conjunction with farina.

RESULTS IN THIRTY-FIVE CASES OF PYLORIC STENOSIS

No.	Name	Age in Wks.	Weight in Lbs. and Oz.	Weight 1 Mo. Later	Ounces Gain in 1 Mo.	Treatment	Result	Remarks
1	Ruth F.	6	5.0	6.12	28	C, Br.	Recovery	Hospital
2	Steph. W.	3	9.8	10.0	8	C, Br.	Recovery	Home and mother
3	Lloyd T.	13	7.8	9.14	28	C	Recovery	Home and mother
4	Harry H.	4	6.4	8.0	28	C	Recovery	Home and mother
5	Claren. T.	14	10.0	11.4	20	C	Recovery	Home and mother
6	Nelson L.	14	8.8	9.8	16	C	Recovery	Home and nurse
7	Robt. D.	10	6.8	7.12	20	C	Recovery	Home and mother
8	John A.	7	8.4	8.4	0	C, Br.	Recovery	Home and nurse
9	John B.	7	6.12	6.12	0	C	Improved	Hospital
10	Betty H.	4	5.4	6.4	16	C	Recovery	Home and nurse
11	Donald F.	3	6.9	6.12	3	C, 0	Recovery	Home and nurse
12	Betty M.	22	11.4	12.12	24	C	Recovery	Home and nurse
13	Rosie R.	12	5.0	7.2	34	C	Recovery	Hospital
14	Nancy B.	5	6.4	6.4	0	0, C	Recovery	Hospital
15	Betty C.	11	7.0	7.0	0	C, 0	Died	Hospital
16	Thos. N.	6	7.14	8.15	17	C	Recovery	Home and mother
17	Blain B.	12	9.8	11.2	26	C	Recovery	Home and mother
18	Norm. S.	12	7.15	9.7	24	C	Recovery	Home and mother
19	Virgin. D.	14	7.12	9.8	28	C	Recovery	Home and mother
20	Henry D.	5	6.8	9.14	54	C	Recovery	Hospital
21	Edw. P.	9	7.0	.....	..	C	Died	Hospital
22	James B.	13	8.12	10.8	28	C	Recovery	Home and mother
23	James C.	8	7.3	10.2	47	C	Recovery	Home and mother
24	Warren P.	7	6.8	9.10	50	C	Recovery	Home and mother
25	John W.	5	6.12	8.8	28	C	Recovery	Home and mother
26	Chas. S.	5	9.1	.....	..	C, 0	Recovery	Hospital
27	Ward P.	3	6.14	.....	..	C, 0	Recovery	Hospital
28	William M.	4	6.9	7.11	18	C	Recovery	Home and mother
29	Jerome R.	6	6.6	.....	..	C, 0	Died	Hospital
30	John Be.	9	10.8	12.4	28	C	Recovery	Home and mother
31	Alene T.	4	6.14	.....	..	C, 0	Recovery	Hospital
32	Everett W.	12	8.4	7.12	..	C	Recovery	Hospital
33	Wm. M.	5	6.9	7.12	19	C	Recovery	Home and mother
34	Clair W.	5	6.8	7.8	16	C	Recovery	Home and mother
35	Edw. N.	7	6.4	7.0	12	C	Recovery	Home and mother

C, thick cereal; 0, operation; Br., breast milk.

This report, covering thirty-five cases of pyloric stenosis, gives the results of all cases seen from 1914-1921 (see table). In a previous communication,[17] the first twelve cases were reported somewhat in detail. Twenty-two of the patients gained a pound or more during the first month. Twenty- four gained from the start. Eighteen were taken care of in the home by the mother. One of my thirty-five patients died while receiving thick cereal. This boy (Case 21) was admitted to the hospital when 9 weeks old weighing 7 pounds. The vomiting decreased as soon as the thick cereal was begun. There was no gain in weight. The child died suddenly on the ninth day. No necropsy was obtainable.

Operative Cases.—Five of the seven operated patients recovered.

17. Sauer: Arch. Pediat. **35**:385, 1918.

CASE 7 (11).—This case is of interest because peristaltic waves were never visible, nor could a tumor be palpated. The projectile vomiting began when the child was 2 weeks old. The vomiting occurred after most nursings. During the first few days, a tablespoonful or more of thick cereal was given before the nursings. As this was without effect, three thick cereal feedings were given, alternating with four nursings. The cereal was retained better than the breast milk, but the weight remained stationary. After another week, six cereal feedings were given, the breast milk being added to the thick cereal. In spite of the best nursing care, decrease in the vomiting and from one to three bowel movements a day, the child failed to gain. The vomiting occurred a few times a day but was very forceful. At operation, a tumor much larger and harder than usually encountered, was incised. The child made an uneventful recovery, being weaned at nine months. Case 14 was one of pyelocystitis

Fig. 10. Case 13. Series B.—Four hours after bismuth farina feeding (stomach nearly empty).

complicating the pyloric stenosis. When first seen, the baby was 5 weeks old and weighed 6 pounds 4 ounces. Her temperature was above 104 F. She was given fluids subcutaneously and by rectum and the Strauss modification of the Fredet-Rammstedt operation was performed a few days later (temperature 102 F.) The vomiting continued for four weeks after operation, although the cystitis had entirely cleared up (temperature normal for several weeks). Having received breast milk for four weeks after operation without a gain in weight, thick cereal feedings were gradually substituted. The vomiting ceased within three days and the child gained 18 ounces during the first month of thick cereal feeding. The operation in this case was inadequate (Fig. 3).

CASE 7. (15).—Betty C., was 11 weeks old and weighed 7 pounds when admitted to the hospital. She was a patient of Dr. H. F. Helmholz. Her

admission temperature of 102 F. was probably due to "influenza." This was followed by a purulent otitis media and a subsequent bronchopneumonia. The vomiting was not very severe, but the roentgen ray showed that the food did not leave the stomach entirely at the end of four hours. As the weight remained stationary during the fifty days of thick cereal feeding, the Fredet-Rammstedt operation was performed under local anesthesia. The child vomited large quantities of blood after operation. She died three days later in spite of two blood transfusions. There was no necropsy.

CASE 8 (26).—Chas. S., was referred by a pediatrician who had tried the thick cereal without result. The child was 5 weeks old and weighed 9 pounds 1 ounce (8 ounces less than at birth). He lost 9 ounces during the twelve days he was under my care. As he seemed to be suffering severe pain, the Strauss modification of the Fredet-Rammstedt operation was performed. Recovery was uneventful.

CASE 9 (27).—Ward P., had projectile vomiting on the fourth day after birth. The vomiting subsided after a few days and the child regained his birth weight (8 pounds 2 ounces) on the sixteenth day when he was circumcised. That night the projectile vomiting was much increased and continued to be very forceful. Peristaltic waves were not very prominent. Roentgenograms taken four hours after a thick cereal feeding showed that very little food passed beyond the pylorus. The child lost 21 ounces in six days. In spite of lavage, bottle breast milk feedings and attempted duodenal feedings the weight continued to decrease rapidly. The Fredet-Rammstedt operation was performed on the twenty-second day. The tumor was not very large and not very hard. Recovery was rapid on breast milk.

CASE 10 (29).—Jerome R., never regained his birth weight as the vomiting began a few days after birth. He was first seen when 6 weeks old, weighing 6 pounds 6 ounces. Thick cereal feedings had been attempted in the rural home by another pediatrician under rather adverse circumstances. When admitted into the hospital his general condition was poor. As he frequently refused to swallow the food and often appeared drowsy he was operated on eleven days after admission. He died rather suddenly two days after operation. No necropsy was obtainable. There were no manifest complications.

CASE 11 (31).—Alene T., was admitted when 4 weeks old, weighing 7 pounds (5 ounces less than at birth). Thick cereal feedings were given for about a week, during which time she lost 6 ounces. As the vomitus frequently contained appreciable quantities of brown blood, she was operated on. She gained rapidly the following week, then a pharyngitis developed which was accompanied by other complications. (For subsequent details see above.)

Some clinicians and surgeons consider the roentgen ray an aid in diagnosis. Others use roentgenography to determine the degree of patency of the pylorus. Downes and Holt [18] consider it of no diagnostic value in typical cases. Strauss believes that a "fluoroscopic examination shows definitely not only if there is a congenital pyloric stenosis, but also if the patient should be treated medically or surgically. If from 70 to 80 per cent. of the bismuth milk goes through within four hours, there will undoubtedly be recovery, irrespective of any clinical symptoms or tumor." The estimation of the amount left in the stomach at the end of four hours requires a lot of experience, to say the least.

Our experience with the roentgen ray in this connection is of exceptional interest. The first case which was subjected to such examination

18. Holt: J. A. M. A. **68**:1517 (May 26) 1917.

is reported here in detail. This girl baby (Case 13) is undoubtedly the most interesting case of the whole series. Pictures were taken also of Cases 15, 16, 20, 27, 31 and 32. Pictures were taken with bismuth milk (Series A) and a few days later with bismuth thick cereal (Series B). The only change made in the formula was the addition of sufficient farina to make it thick. Roentgenograms were made with the patient in the position advocated by Strauss, also with the infant lying on the back. Roentgenograms were taken immediately after the feedings, also one, two and four hours later.

The first series shows that most of the bismuth milk was still in the stomach at the end of four hours, irrespective of the position of the child. In the second series, the same food, thickened with farina, quickly passed into the duodenum and the stomach was nearly empty at the end of four hours. This infant, according to Strauss' standard, would need operation. She was not operated on, but was given thick cereal and gained 34 ounces in thirty days (Fig. 4). She died of gonorrheal peritonitis some months later. A typical, cartilaginous hypertrophy of the pylorus was found,[19] in spite of the fact that she had been absolutely free from feeding disturbance.

When the diagnosis of pyloric stenosis is made the author tells the parents the nature of the ailment and that an operation may be necessary, but that thick cereal feedings will be tried for a short time to see whether the symptoms improve. The general condition of the patient, the stools, urine, vomitus, weight, food and feeding technic are closely watched. The presence of a palpable tumor or the size of the peristaltic waves have no bearing in making a decision. The weight, severity of vomiting, paucity of fecal material, complications and the general condition of the patient are the factors that determine how long thick cereal feedings may be tried. Fluids, preferably 6 per cent. dextrose Ringer's solution, are always given regularly by rectum or subcutaneously. If, after a thorough trial (from one to two weeks) the vomiting fails to subside, if the weight fails to increase, or if the general condition of the child gets worse, operation is resorted to. In some cases conditions may be such that early operation may be advisable, for example, when infants come under observation in a very emaciated state and fail to respond immediately to the treatment.

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19. Ibrahim, Wernstedt,[20] Bloch,[21] Batten,[22] Simon[23] and others have reported cases of known pyloric stenosis in which the patient died months or years after recovery without operation, but in which the cartilaginous tumor persisted.

20. Wernstedt: Jahrb. f. Kinderh. 674, 1907.

21. Bloch: Jahrb. f. Kinderh. 337, 1907.

22. Batten: Lancet 1511, 1899.

23. Simon: Jahrb. f. Kinderh. 331, 1911.

With so much still unexplained about the mechanism of the normal pylorus, it is impossible to give a satisfactory explanation of how the thick cereal passes into the duodenum in case of pyloric stenosis while the same food thinned out (to reduce its consistency) is promptly vomited. Moritz [24] found that in the adult solid food inhibited, and water stimulated gastric peristalsis. Schüle [25] found fluid foods to increase the motility of the stomach. If one watches the events with the fluoroscope after ingestion of bismuth thick cereal it is seen that the mass gravitates to the pylorus and that more material passes through in a given time than with bismuth milk.

SUMMARY

1. The use of thick cereal in thirty-five cases of pyloric stenosis brought about a rapid gain in weight in twenty-four cases and was effective in twenty-eight of the thirty-five cases.

2. The preparation and administration of the food are important.

3. Patients should be operated on if the thick cereal fails to bring about improvement in from one to two weeks. Under certain conditions, one should not wait too long before operation.

4. Complications following operation are not infrequent.

5. Thick cereal feedings may be valuable when vomiting continues after operation.

CONCLUSION

In cases of pyloric stenosis proper medical treatment, supported, when necessary, by proper operative treatment, will give the best results.

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24. Moritz: Ztschr. f. Biol. **42**:572, 1901.
25. Schüle: Ztschr. f. klin. Med. **29**:73, 1896.

CONGENITAL ANEURYSMAL DILATATION OF DUCTUS BOTALLI*

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The heart described in this paper has a patulous ductus arteriosus which is dilated to the extent of being aneurysmal. In my experience this is a most unusual finding, and so few instances are recorded that the case is worthy of report.

REPORT OF CASE

Baby E., male 3 days old, one of twins born spontaneously in the Jefferson Hospital Maternity Department, service of Prof. E. P. Davis, was undersized and weak, but there was no external evidence of faulty development; the weakness progressed until death occurred. Diagnosis: general debility. The other twin, a female, was of normal size and weight and apparently healthy; so far as I know this child is strong and well. The mother, white, aged 26, is engaged in general housework. Her family history contains no point bearing on this case. Her personal history is negative. She has had one previous normal pregnancy and the child is living and well. No miscarriages or stillbirths. Evidence of syphilis lacking; Wassermann test not made.

Necropsy, Twenty Hours After Death.—Body is that of a poorly nourished, white male infant, 46 cm. in length; weight, 2.5 kilos. Rigor mortis absent. No external abnormality. Fontanelles, interosseous cranial sutures, umbilical stump, scrotum and orifices normal. Heart measures 4 by 3 by 2.5 cm.; weight, 10 gm. Chambers, walls and valves, normal; foramen ovale closed. Between the pulmonary artery and aorta, a short distance above their exit from the ventricles, an ovoidal, fluctuating, apparently cystic mass is noted. In size it compares with a large cherry, and on incision contains a small amount of recent free blood clot. At each end of the mass is an opening communicating with the aorta on the inferior aspect of the arch, on the one hand, and the pulmonary artery slightly above and to inner side of left branch on the other. The wall of the dilated central portion is very thin, and the inner surface is smooth and regular; it measures 17 mm. in length and 11 mm. in its greatest diameter. The orifice at the aortic end is 5 mm. in diameter, and the one at the pulmonic end is 3 mm. The aorta and pulmonary artery each measure 5 mm. in diameter. At the junction with the aorta, the wall is smooth and regular, without a sign of the valvular fold occasionally seen in this region. The aortic and pulmonary valve orifices are normal, as well as the leaflets closing them. There is no stenosis or atresia of the main arteries or their branches beyond the dilated communication between them.

The lungs are slightly congested at their bases, but show evidence of previous complete expansion. The thymus apparently is normal. Other findings are irrelevant.

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* Received for publication April 28, 1921.

* This article was prepared by Dr. Dry and found among his papers after his death. With slight revision it is presented as the last piece of work done by a conscientious, able and enthusiastic man whose professional career—a most promising one—was ended by an incurable malady to which he succumbed in September, 1917. Dr. Dry had been demonstrator of morbid anatomy in Jefferson Medical College. (W. M. L. C.)

DISCUSSION

Anatomically, the ductus arteriosus is a tube from 10 to 15 mm. in length, extending from the left branch of the pulmonary artery directly after its bifurcation, to the under side of the arch of the aorta just beyond the origin of the left subclavian artery. Its diameter has been recorded as being from 4 to 7 mm. These wide variations are due to the fact that different observers have studied it under different degrees of distention. Klotz,[1] who injected a number of arteries in the newborn, found the ductus arteriosus equal in size to the main pulmonary trunk. The small diameters recorded were noted after firm contraction of the muscle wall.

Natural size of specimen. A. Thoracic aorta and part of abdominal aorta, opened and turned upward. B. Pulmonary artery. White rod passed from main trunk out through left branch. C. Ductus arteriosus opened longitudinally, showing interior of aneurysmal sac.

After birth it undergoes rapid involution, the lumen being practically impermeable by the third week of extra-uterine life. Changes which lead to permanent obliteration, however, go on for some months and form the ligamentum arteriosus of later life. While this is the natural sequence, it is, nevertheless, a fact that in a certain number of cases this duct never closes or is only partially closed, or in a still smaller percentage, actually becomes dilated.

1. Klotz: Tr. Ass. Am. Phys., 1907.

Persistent patulous ductus arteriosus, next to persistent patulous foramen ovale, is the most frequent congenital cardiac defect. In Maude E. Abbott's [2] analysis of 631 cases of congenital cardiac diseases, the duct was patulous in 166, 64 of which were unassociated with other cardiac defects, 102 accompanied other cardiac anomalies. A patulous duct may be of normal size; it may be narrower and shorter than normal, or it may be a canal which has undergone aneurysmal dilatation. Of this last group, Maude E. Abbott [2] records only fourteen cases, thirteen were unassociated with other cardiac defects, one was associated with other cardiac defects. These figures, together with the almost total absence of reported cases in the literature, prove that while patency of the duct is not rare, this type of aneurysmal dilatation is most uncommon. The early reported cases were seen by French writers. Rokitansky, in 1852, described what is taken to be the classical form, "a spherical or ovoid tumor larger at the middle than at either end, but smallest toward the pulmonary artery, with which, as well as with the aorta, it communicates, filled with old or recent thrombus and varrying in size from a cherry stone to a hazelnut or even a walnut."

In 1856, Virchow reported a case in which the duct was dilated in the middle to the size of a cherry with an opening into the pulmonary artery of pinhead size, and one into the aorta, the size of a pea. This aneurysm was filled by a thrombus, the pointed end of which projected into the aorta. Hebbs [3] reported a case in a man, aged 40, in which the opening was the size of a walnut. Weller [4] reported a case in an infant, 5 days old, in which it was the size of a cherry.

What is the cause of patency and dilatation of the ductus arteriosus? Naturally, one tries to explain this by the absence of these factors responsible for obliteration of the duct, and in so doing, finds that the hypotheses advanced are many and most of them little more than speculation.

1. Langer, Walkhoff and Thoma,[5] Kautsch [6] and Klotz [1] agree that the duct wall is deficient in elastic tissue as compared with the aorta and pulmonary artery, but is relatively rich in muscle. According to Thoma [5] a loose subintimal layer of muscle is present which corresponds to Jore's musculo-elastic layer of the arterial wall. This is developed earlier and to a greater extent than in the aorta and pulmonary artery. It is more prominent at each end of the duct and

2. Abbott, Osler-McCrae: Mod. Med. **4**:342.
3. Hebbs: Tr. Path. Soc. Lond. **44**:45, 1893.
4. Weller: Bull. Internat. Ass. Med. Museums **5**:1915.
5. Langer, Walkhoff and Thoma: Arch. f. path. Anat. **93**: 1883.
6. Kautsch: Halle, Diss. 1896 (Quoted by Gruner).

passes into and forms the musculo-elastic layer of the aorta. Histologically, therefore, the occlusion might be attributed to contraction of the prepondering muscle.

2. At birth definite alterations in blood pressure occur. Previous to birth the pressure is highest on the right side of the heart and practically all the blood passes through the ductus into the aorta. At birth, the lungs are expanded, their capillaries are opened simultaneously and the pulmonary blood pressure is lowered. Landau supposed there was an active aspiration of blood into the pulmonary artery with the first breath, a resultant negative pressure and collapse of the duct. Schultze maintains that closure takes place at the moment when the pressure in the aorta becomes equal to that in the pulmonary artery, so that the blood in the ductus arteriosus stagnates, and that this event may take place immediately or some days after birth, and that closure is made permanent by an annular contraction of the ductus. Adami [7] says that for some little time after birth the aortic tension, and, therefore, the mean blood pressure in the body, is lowered, owing to the reduced amount of work which the heart performs after exclusion of the placental circulation, and that lowering of the mean blood pressure is the main factor in the closure of the duct.

3. At birth there are definite alterations in position of the ductus relative to the great vessels. Schantz states there is stretching by initial respirations. Walkhoff maintains that a bending and slowing of the stream favors thrombosis and organization. Strassmann [8] describes a fold in the aortic wall in the upper border of the mouth of the duct which acts like a valve when pressure rises in the aorta at birth. The fact remains, and is notably disputed by Sharpe, that the fold is not constant. In Wagner's three cases of patency it was markedly developed.

As to that portion of the duct which becomes obliterated first there is also much variance of opinion. Peacock [9] says closure of the duct commences at the aortic extremity and gradually advances toward the bifurcation of the pulmonary artery. Klotz [1] finds contracture most marked at the ends, and this view is supported by the bean-shaped form seen in the aneurysmal dilatations. Langer [5] says the obliterating process begins at the middle and progresses first toward the pulmonary and then toward the aortic end.

In the case reported herewith, there is slight contraction at both extremities, most marked at the pulmonary end. The wall of the dilated portion was very thin, and that part examined histologically was made up of a thin layer of muscle and practically no elastica; the

7. Adami, Osler-McCrae: Mod. Med. **4**:411.
8. Strassmann: Arch. f. Gynäk. **45**: 1894.
9. Peacock: Malformations of Human Heart, 1858-1866.

intima was absent. There was no evidence of thrombus formation within the duct. The aorta showed no valvular fold around the duct orifice. The condition of the lungs, pulmonary artery and aorta was such as to cause only normal alterations in blood pressure.

Is the term aneurysm justifiable? If one accepts the general definition of aneurysm as a dilatation of the walls of an artery, or if one is even less liberal and accepts the more restricted definition, as any pathologic widening of the arterial lumen caused by change in its walls, one must class this as a distinct aneurysm. Undeterminable as it may be, there is some underlying pathologic condition in either the mother or during intra-uterine life, that has occasioned this weakening of the wall. We have accepted the possibility of congenital aneurysms in other large arteries, and why, therefore, is it not possible in the ductus arteriosus, where the factor of stress in intra-uterine life is as great or greater than in many other arteries?

While most reported cases occurred in infants, Hebbs' case, which occurred in a man, aged 40, proves that the condition is not necessarily incompatible with life and with apparent health—at least it produces no more serious results than do other lesions that permit admixture of venous and arterial blood. In none of the reported cases has the cause of death been attributed directly to the aneurysm.

Recognizing the condition as an aneurysm, we must remember that it is liable to the same changes as any other aneurysm. Its possibilities of rupture, pressure on surrounding tissues, thrombus formation within and healing or the softening of the thrombus at any time settling free emboli, must be considered as of vital importance to the patient and of distinct clinical interest, and secondary pathologic changes are not only possible but highly probable.

CONCLUSIONS

1. This is one of the few cases of dilatation of a patulous ductus arteriosus.

2. The dilatation is such as warrents its being classed as an aneurysm.

3. The dilatation is thought to be due mainly to deficient muscular development in the walls of the ductus.

4. This case conforms to the classical type described by Rokitansky, except that it did not contain a thrombus.

5. Due to the fact that such aneurysms may occasionally rupture or undergo other important changes, it is of sufficient clinical and pathologic interest to record.

AN INTERPRETATION OF THE SEASONAL VARIATION OF RICKETS

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The Medical Research Committee of Great Britain, in its report on rickets, published in 1918, came to the conclusion that "in spite of a most varied and extensive research we have practically no real knowledge of the nature or causation of this widespread malady, or of the factors which determine its onset." [1] There are two widely divergent theories as to its etiology—the hygienic and the dietetic, the pendulum swinging sometimes in the one and sometimes in the other direction. As will be remembered, Kassowitz, one of the best known students of this disorder, maintained the opinion that rickets came about from breathing noxious gases, which accumulated in badly ventilated rooms.[2] Von Hansemann ascribed its development to "domestication," including under this broad term all the harmful influences which result from modern civilization.[3] Findlay and Paton, in the report just referred to, emphasize the etiologic importance of inadequate air supply and exercise. On the other hand, the dietetic point of view has been maintained by a large number of clinicians and laboratory investigators ever since the days of Glisson. Its most recent advocate has been Mellanby,[4] who came to the conclusion that a vitamin (the fat-soluble vitamin or one closely resembling it) is the paramount factor in the causation of this disorder. This opinion has gained recognition and acceptance with surprising rapidity. It was at once adopted by the Medical Research Committee of Great Britain in a report issued in 1919 [5] and has gained an established place, even in textbooks on medicine and pediatrics.

As is well known, rickets is a disorder which is most prevalent among the poorer classes and is met with far more frequently among infants in cities than among those in the rural districts. There is some difference of opinion as to its frequency, but all seem to agree that it occurs in more than 50 per cent. of the children of the poor. In his well known investigation, which was based on pathologic rather than

1. Medical Research Committee: A Study of Social and Economic Factors in the Causation of Rickets. Special Report, Series No. 20, London, 1918.
2. Kassowitz, M.: Praktische Kinderheilkunde, Berlin, 1910.
3. v. Hansemann, D.: Berl. klin. Wchnschr. **629**:670, 1906.
4. Mellanby, E.: Lancet **1**:407 (March 15) 1919.
5. Medical Research Committee: Report on Accessory Food Factors. Special Report, Series No. 38, 1919.

on clinical data, Schmorl found rickets in 89 per cent. of hundreds of cases.[6] The recent book of Thomson on sick children gives its occurrence as being over 50 per cent. among the children of Edinburgh, London, Glasgow and Manchester, and states that "had roentgen-ray examination been used, a much larger proportion would certainly have been recognized." [7]

As emphasized in a recent paper,[8] season plays a most remarkable rôle in the incidence of this disorder. In this respect, rickets can be compared almost to pellagra, which comes into sudden prominence in the spring and rapidly disappears from view in the early summer. To a less extent this is true of beriberi, tetany and scurvy. This striking seasonal incidence of rickets is acknowledged by all, by clinicians as

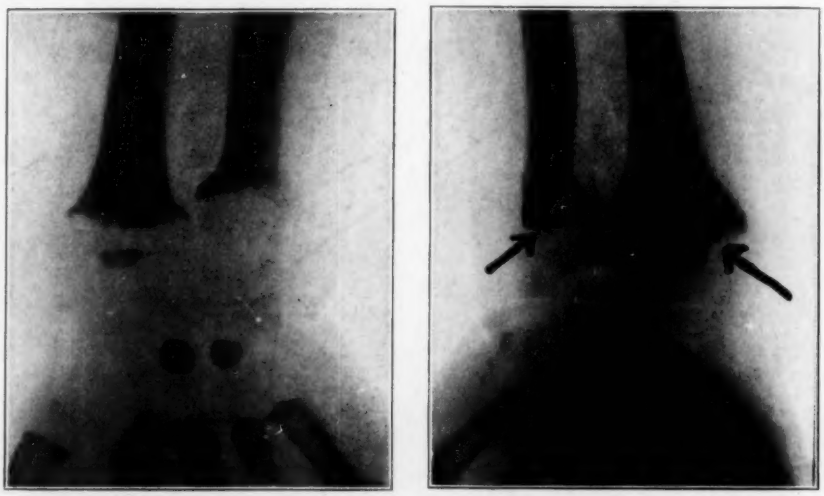

Fig. 1.—F. W. (18 months). Two roentgenograms of the same infant, one showing rachitic changes of the epiphyses and the other calcification following ultraviolet ray therapy (arrows).

well as by pathologists. It, therefore, becomes a matter of importance in unraveling the etiology of this disease to attempt to gain an insight into the factors leading to this increase of rickets during the winter and early spring and its decrease during the summer months. These seasonal phases have been subjected to two interpretations, quite differ-

6. Schmorl, G.: Die pathologische Anatomie der rachitischen Knochenerkrankung, Ergebn. d. inn. Med. u. Kinderh. **13**:403, 1914.

7. Thomson, J.: Clinical Study and Treatment of Sick Children, Oliver and Boyd, Edinburgh, 1921.

8. Hess, A. F.: Newer Aspects of Some Nutritional Disorders, J. A. M. A. **76**: 694 (March 12) 1921.

ent in their nature. Some believe that climate is the determining factor, whereas others attribute the rise and subsidence to alterations in the food, which occur in the course of the changing seasons. At present, the dietetic theory of rickets holds sway, and the majority of clinicians and investigators have taken it for granted that diet is the preponderating factor in its incidence, and likewise is responsible for its seasonal variation.

In the course of our experience in a large child-caring institution, rickets has been found to occur with every food, without exception. Cases have developed when the dietary contained a large quota of milk, and therefore was rich in fat; when fat and the fat-soluble vitamin

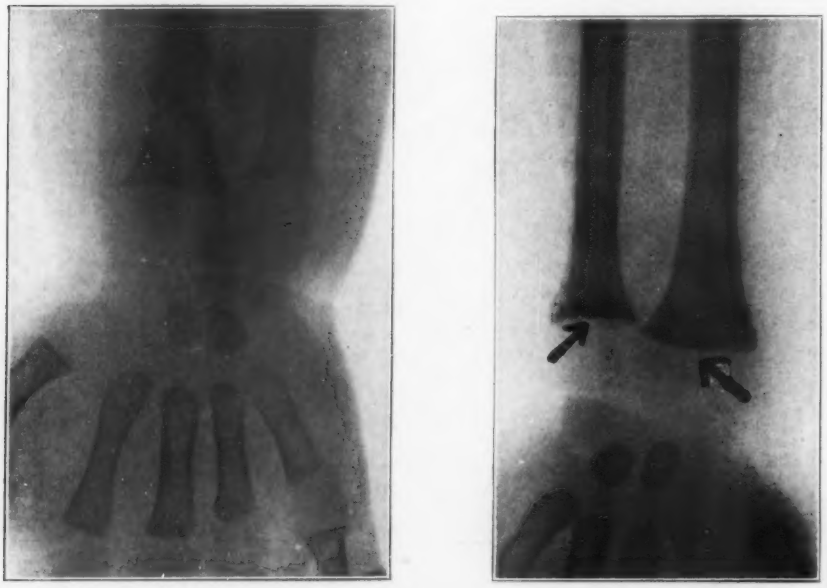

Fig. 2.—H. B. (21 months). Roentgenograms showing rachitic changes in the epiphyses (left) and calcification following eight weeks' treatment with ultraviolet ray (right).

were lacking in the diet; when the milk was raw or pasteurized. It has been noted on a diet of fluid milk, dry milk, condensed milk, protein milk and human milk.[9] On every one of these dietaries some babies have developed rickets, whereas others have remained perfectly normal in this respect. This peculiar phase of the etiology we shall,

9. The most marked instance in the institution today is that of a child which is being nursed by its mother, who is receiving an ample diet, which includes over a quart of milk a day. It may be noted in this connection that some years ago we found that fully one third of the negro babies who were nursed showed definite clinical signs of rickets.[10]

10. Hess, A. F., and Unger, L. J.: The Diet of the Negro Mother in New York City, J. A. M. A. **70**:900 (March 30) 1918.

however, discuss at some future time. In referring to rickets, we have in mind cases which showed the typical picture on roentgen-ray examination and, for the purposes of the present discussion, have excluded such cases as showed signs merely on inspection or palpation.

In a study of experimental scurvy of guinea-pigs, it was shown by us, as well as by others, that milk differs greatly in its antiscorbutic content according to the fodder of the cows;[10] that if the animals have been on a diet very poor in antiscorbutic vatamin for a period of three weeks, the milk which they secrete is, from a dietetic standpoint, almost devoid of this vitamin. It seemed, therefore, possible if, as has been predicated, rickets is likewise a deficiency disease, dependent on a lack of an "antirachitic vitamin," that its marked occurrence in the winter might be associated with the fodder of the cows, resulting in a lack of this specific factor in the milk. We, therefore, made an effort to rectify the possibility of such a deficiency, by obtaining dry milk which had been prepared during the summer from the milk of pasture-fed cows. A sufficient quantity of this milk was secured for eight of the twenty infants who were receiving a diet of dry milk.

In our experience dry milk is a most valuable infants' food and has not been associated with the development of rickets. Such also has been the experience of others. For instance, Koutts, as the result of his inquiry for the Local Government Board of England, recommended its use in infant feeding, stating that rickets was of rare occurrence with this type of feeding;[12] indeed, he cited numerous cases in which a cure was effected by substituting dry for fluid milk. Winfield, in the same report, in a consideration of the "nutritive value of dried milk," concluded that cow's milk during the process of desiccation "loses none of the characters which are necessary for the support of the normal growth of infants."

Two of the eight infants fed on this dry "pasture milk" showed some rachitic changes on roentgen-ray examination, although their general condition was good, and they had gained steadily in weight. Just why these two children should have developed rickets we do not know; this question of individual susceptibility has been and is one of the enigmas of this puzzling disorder. On reviewing the welfare of the other infants who were fed on dry milk throughout the winter, but who received the ordinary commercial product made from the milk of stall-fed cows, we find neither a greater nor lesser incidence of rickets.

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11. Hess, A. F., Unger, L. J., and Supplee, G. C.: Relation of Fodder to the Antiscorbutic Potency and Salt Content of Milk, J. Biol. Chem. **45**:229, 1920.

12. Koutts, F. J. H.: Upon an Inquiry as to Dried Milks, etc. Report to Local Govt. Board, New Series 116, 1918.

Among these, three infants developed mild rickets, whereas the remaining nine showed normal epiphyses on roentgen-ray examination. It will be noted, therefore, that the ratio was the same among those fed what may be termed "pasture milk" and those obtaining the winter or "stall-fed milk." [13]

The logical deduction from this experience seems to be that the milk of cows supplied with green fodder does not acquire antirachitic properties, and that rickets develops in infants during the winter months, irrespective whether milk from pasture-fed or stall-fed cows is given. It should be borne in mind that the brand of milk which we used, prepared by the Just roller process, contains a large amount of all of the three established vitamins—the fat-soluble, the water-soluble, and the antiscorbutic.

CURATIVE EFFECT OF ACTINIC RAYS

In 1917, in considering this problem, we attempted to cure rickets by means of the ultraviolet rays [14]—the first attempt, as far as we are aware, of employing these rays in this connection. It seemed that if "season" were to be interpreted as a climatic influence, in which the sun plays an important rôle, artificial actinic rays might bring about a similar effect. Accordingly, we made use of the mercury vapor lamp, which produces short rays of less than 300 microns in length. The results were not definite. At that time we did not follow the progress of the cases by means of the roentgen-ray, as we have done for the past year or more, so that it was difficult to observe slight and prompt evidences of calcification. In the interval, Huldschinsky reported favorable results with these rays.[15] He did not, however, control the diet in his cases, and in very many instances gave calcium phosphate or cod liver oil in addition, so that it is difficult to determine to what extent dietetic factors influenced his results.

As we now have the roentgen-ray at our disposal, we determined to test again the value of the ultraviolet ray therapy. Six infants who had a mild degree of rickets and were on various diets were selected for treatment. They had developed rickets on diets of "pasture dry milk," malt soup, condensed milk, breast milk, etc. The treatment was given three times a week and continued for a period of about two months.

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13. In passing it may be mentioned that some of the very best certified milk sold in New York City is the product of cows which are stall-fed all the year round. They are not allowed to graze, for fear of their eating herbs which might transmit a disagreeable flavor to the milk.

14. Hess, A. F. and Unger, L. J.: The Clinical Rôle of the Fat-Soluble Vitamin: Its Relation to Rickets. J. A. M. A. **74**:217 (Jan. 24) 1920.

15. Huldschinsky, K.: Die Behandlung der Rachitis durch Ultraviolett bestrahlung. Ztschr. f. orthop. Chir. **89**:426, 1920.

The entire body was exposed to the rays, at first for a period of about three minutes, the length of exposure being increased gradually to twenty minutes. The distance of the lamp from the body was likewise gradually lessened; at the beginning it was placed about 120 cm. from the body, being set a few centimeters nearer each time until it was 75 cm. distant. The infants, who varied in age from 8 to 21 months, seemed to enjoy the rays and became increasingly tanned, although by no means so brown as under the more intensive treatment in 1917. Their hemoglobin percentage and number of red cells increased in every instance. In all cases, the rickets showed definite improvement as evidenced by roentgen-ray examination. The earliest beneficial effect was noted in two cases in twenty-six days, after seven treatments had been given; in these instances a definite deposition of salts

TABLE 1.—ULTRAVIOLET RAY TREATMENT

Name	Age, Mos.	Diet	Total Number Treatments	Rickets by Roentgen Ray					
				Date, 1921	Raying Begun	Date, 1921	Raying Continued	Date, 1921	Raying Ended
E. B.	8	Farina, dry milk (summer), orange juice	25	2/3	Moderate	3/ 3	Healing	4/ 5	Healed
H. B.	21	"Malt soup," farina, orange juice	22	2/3	Moderate	3/ 3	Calcification	4/ 5	Healed
F. W.	18	Sweetened condensed milk, farina, orange juice	19	2/3	Moderate	3/ 3	Moderate	3/29	Marked healing
A. R.	10½	Dry milk (winter), farina, orange juice	10	3/3	Slight	3/29	Calcification	4/ 5	Healing
B. H.	9	Farina, protein milk, yeast, orange juice	10	3/3	Slight	3/29	Healed	4/ 5	Healed
F. H.	5½	Breast milk	8	4/1	Moderate	4/20	Calcification		

was apparent at the epiphyseal ends of the ulna and radius. In two other cases, after the treatment had been continued for less than eight weeks, the roentgenogram showed a striking healing process (Fig. 1). It will be remembered that there was no change whatsoever in diet throughout these periods. It must also be borne in mind that this improvement occurred in all infants during the months of February and March; in other words, when rickets is wont to manifest its highest incidence and is least apt to decrease in severity.

We have no means of knowing how this deposition of salts is brought about—whether by direct action or through the medium of some intermediate factor. The effect is undoubtedly systemic and not the result merely of a local action on the epiphyseal ends of the bones. Whatever its nature, such a result indicates that the influence of light must be considered in planning and interpreting metabolism studies

involving estimations of the inorganic salts. It shows also that in rickets a deposition of salt into the bones may be accomplished without any addition or alteration in the diet. The only chemical data we have been able to find, which illustrate the influence of rays on the metabolism of inorganic salts are furnished by an investigation of Raczynski. He took two puppies of the same litter, both of which were being suckled by the mother, and kept one in absolute darkness and the other, throughout the day, in sunlight. At the end of a six weeks' period both were killed. An analysis of their bodies showed that the one which had been reared in the sunlight contained over 50 per cent. more calcium and 25 per cent. more phosphorus than the other, but that on the contrary, it contained less than half the quantity of chlorin.[16] These chemical analyses are in harmony with the chemical results we have recently reported, which show that sunlight of itself is capable of bringing about a marked cure of rickets. (The diet at all times remaining unchanged.[17])

The chief significance which we wish to draw from our study is an elucidation of the seasonal incidence of rickets. Naturally, it suggests that therapeutic advantage should be taken of the beneficent effect of sunlight—or of ultraviolet rays, when sun is not available—in the prevention and cure of rickets. It helps also to explain why rickets preponderates in the large cities where the infants are closely housed throughout the winter. In regard to the hygienic factor, it stresses the importance of sunlight rather than "fresh air and exercise," which was emphasized in the report of Findlay and Paton.[18]

CONCLUSION

Milk from pasture-fed cows (summer milk) failed to prevent the development or to decrease the incidence of rickets during the winter.

On the other hand treatment with ultraviolet rays or with sunlight brought about calcification of the bones during the winter as demonstrated by means of the roentgen ray. These contrasting results lead to the conclusion that hygienic factors, especially sunlight, and not dietetic factors, play the dominant rôle in the marked seasonal variation of this disorder.

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16. Raczynski, J.: Compt.-Rend. de l'Ass. Internat. de Pediat., Paris, 1913, p. 308.

17. Hess, A. F., and Unger, L. F.: J. A. M. A. **77**:39 (July 2) 1921.

18. It seems probable that the exceptional incidence of rickets among negro infants in New York and other northern cities is attributable, in part, to the pigmentation of their skins, which, as is well known, prevents the penetration of the short actinic rays. By actually passing light through pigmented skin, Sambon and others have shown that the ultraviolet or short waves are filtered out in direct proportion to the density of the pigmentation.[19]

19. Sambon, L. W.: J. Trop. Med., Feb. 15, 1907.

STUDIES OF INFANT FEEDING

XIII. THE CASEINS OF COW'S MILK AND HUMAN MILK IN THEIR RELATION TO INFANT FEEDING. THE ACTION OF RENNIN ON CASEIN *

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It has been quite generally thought that the caseins in cow's milk and human milk have individual characteristics, this idea being based on the observations that the acid and rennin coagulation of the two milks are quite different. While these observations are correct, the interpretation of them, as demonstrating differences in the properties of the two caseins, is open to question in that the salt content of the two milks have not been taken sufficiently into consideration as a factor in the interpretation of the phenomena noted.

Van Slyke and Bosworth [1] have prepared and examined pure casein from cow's milk, and Bosworth and Giblin [2] have done the same with the casein of human milk. With these data at hand, we are enabled now to make more definite statements as to the properties and composition of the two caseins.

Preparation of Caseins.—A brief outline of the method of preparing casein is as follows: The fat is first removed from the milk by centrifugal force and the casein is then precipitated by the careful addition of very dilute acetic acid. With cow's milk the casein separates out in large flakes and soon settles to the bottom of the vessel, permitting the removal of most of the liquid by means of a siphon. With human milk the casein separates out in very fine particles which remain suspended for some time, and in order to separate the liquid, the milk is centrifugalized. After the casein has been separated from the mother liquid, it is washed twice with distilled water and then dissolved in distilled water to which a little ammonia has been added, enough water being used to give about a 0.5 per cent. solution of casein. The casein is again precipitated by the addition of dilute acetic acid. At this stage both caseins now separate out in large flakes. The washing, redissolving and reprecipitating is done several times; the final precipitate, after being washed with water, is washed with alcohol, then with ether, and finally dried in a vacuum dessicator

* Submitted for publication March 18, 1921.
* From the Boston Floating Hospital Laboratories.

1. Van Slyke, L. L., & Bosworth, A. W.: J. Biol. Chem. **14**:203, 1913.

2. Bosworth, A. W.: J. Biol. Chem. **20**:707, 1915; Bosworth, A. W., and Giblin, L. A.: J. Biol. Chem. **35**:115, 1918.

over sulphuric acid. In the case of cow's milk, a special treatment with ammonium oxalate is necessary in order to remove the last traces of calcium. After the initial precipitation from the milks, the two caseins behaved alike in all respects.

Composition of Caseins.—The preparations thus secured were found to have nitrogen, phosphorus and sulphur contents, calculated to the moisture free basis, as noted below, the figures seeming to indicate that the casein from the two milks have the same chemical composition.

TABLE 1.—NITROGEN, PHOSPHORUS AND SULPHUR CONTENT OF CASEINS

	Cow,[1] per Cent.	Human,[2] per Cent.
Nitrogen	15.80	15.75
Phosphorus	0.71	0.70
Sulphur	0.72	0.70

Compounds Formed by the Combination of Casein With Bases.—It has been found that the two caseins are acids, having a valency of eight, and form the same series of salts with bases. As the caseins have a valency of eight, it is theoretically possible to form eight salts.

The first seven of these salts are acid toward phenolphthalein and the last one, octabasic caseinate, is neutral towards this indicator. All sodium, potassium or ammonium caseinates are soluble in water but are precipitated as calcium caseinate on the addition of sufficient

TABLE 2.—SALTS FORMED BY THE COMBINATION OF CASEINS WITH BASES

Name	C.c. of Tenth-Normal Alkali Required for 1 Gm. Casein
1. Monobasic caseinate	1.125
2. Dibasic caseinate	2.250
3. Tribasic caseinate	3.375
4. Tetrabasic caseinate	4.500
5. Pentabasic caseinate	5.625
6. Sextabasic caseinate	6.750
7. Septabasic caseinate	7.875
8. Octabasic caseinate	9.000

amounts of any soluble calcium salt, such as calcium chlorid, this precipitation being due to a double decomposition:

$$\text{Casein } Na_8 + X\ (CaCl_2) \rightarrow \underset{\substack{\text{Insoluble}\\ \text{in presence}\\ \text{of excess}\\ \text{calcium chloride.}}}{\text{Casein } Ca_4} + 8\ (NaCl) + (X\text{-}4)\ CaCl_2$$

The calcium caseinate containing one equivalent of calcium (casein$_2$ Ca) is insoluble in water. All the other calcium caseinates are soluble in distilled water. All the soluble calcium caseinates are precipitated from solution by the addition of a sufficient amount of any soluble calcium salt, the precipitation probably being due to a repression of the

dissociation of the calcium caseinate.[3] The amount of soluble calcium salt required to precipitate the calcium caseinate from solution increases in proportion to the amount of calcium combined with the casein. The dicalcium caseinate will be precipitated by the addition of a trace of soluble calcium while a solution of the octacalcium caseinate will require the addition of appreciable amounts of soluble calcium to cause precipitation.

The Condition of Casein in Milk.—In perfectly fresh cow's milk the casein is present as octacalcium caseinate, the compound neutral to phenolphthalein. In this compound 1 gm. casein is combined with 9×10^{-4} gm. equivalents of calcium, or, in other words, 1 gm. casein is combined with 0.0178 gm. calcium (equivalent to 0.0252 gm. of calcium oxid.[4]

In perfectly fresh breast milk, the casein is present as a caseinate neutral to phenophthalein, but owing to the small amount of casein present in breast milk and the low mineral or ash content of this milk, an exact determination of the nature of the base or bases combined with the casein has not so far been accomplished. It seems quite probable, however, that the casein in this milk is combined with two bases, calcium and potassium.[2]

The Action of Rennin on Casein.—Hammersten was the first to show that the coagulation of milk was due to the action of a soluble ferment which acts directly on the casein, producing, as he thought, two substances, the insoluble curd (Käse), which we call paracasein, and a soluble product which he called whey-protein (Molkeneiweiss). My recent work[5] has shown that the action of rennin on the casein of cow's milk produces a splitting of the casein into two similar molecules of paracasein, perhaps in somewhat the same manner that two molecules of dextrose are produced from one molecule of maltose by enzymatic action. Bosworth and Giblin have also found the same to be the result when rennin acts on the casein obtained from breast milk.[2] These investigations of rennin action seem to prove that Hammersten's whey-protein is not one of the products formed when paracasein is produced by the action of rennin on casein but that this whey protein is due to the continued action of the proteolytic enzyme on the paracasein, soluble compounds not precipitated by the action of rennin or acids being produced. In other words, we do not believe that there is a distinct ferment rennin but that the action commonly attributed to this ferment can be produced by any proteolytic ferment.

There has always been considerable doubt as to whether the curdling of milk by enzymatic action is due to a distinct ferment rennin

3. Robertson, T. B.: J. Biol. Chem. **2**:381, 1907.
4. Van Slyke, L. L., and Bosworth, A. W.: J. Biol. Chem. **20**:135, 1915.
5. Bosworth, A. W.: J. Biol. Chem. **15**:231, 1913; **19**:397, 1914.

or whether this power to curd milk is an attribute possessed by all proteolytic ferments. The author is inclined to believe that rennin action is a hydrolytic cleavage and may be considered the first step in the proteolysis of casein. It would follow from this that the action now attributed to rennin may be produced by any proteolytic enzyme. The figures given in Table 3 support this view. It will be noticed that the paracaseins produced by the action of rennin and trypsin not only have the same percentage composition but that this composition is the same as that of casein.

TABLE 3.—SHOWING COMPOSITION OF CASEIN AND PARACASEINS[3]

		Paracasein	
	Casein	By Rennin	By Trypsin
Carbon	53.50	53.50	53.47
Hydrogen	7.13	7.26	7.19
Oxygen	22.06	21.94	22.04
Nitrogen	15.80	15.80	15.78
Phosphorus	0.71	0.71	0.71
Sulphur	0.72	0.72	0.72

The Chemical Properties of Paracaseinates.—A study of the chemical properties of the paracaseins produced from the caseins of cow's milk and breast milk shows them to be alike in the following respects:

1. They are acids.
2. They have a molecular weight of 4444, one half that of casein.
3. They have a valency of 4, one half that of casein.
4. The paracaseins form a series of four salts as follows:

	C.c. of Tenth-Normal Alkali Required for 1 Gm. Paracasein
(1) Monobasic paracasein	2.25
(2) Dibasic paracasein	4.50
(3) Tribasic paracasein	6.75
(4) Tetrabasic paracasein	9.00

The first three of these salts are acid toward phenolphthalein and the last one is neutral toward this indicator.

5. Paracasein, when produced by the action of rennin in solutions of ammonium, sodium or potassium caseinates, does not result in a curd as the paracaseinates of these bases are soluble.

6. A solution of calcium caseinate containing four or more equivalents of base and free from all other salts is not curdled by rennin. In such a solution, however, the caseinate is changed to a paracaseinate; this paracaseinate being soluble in the absence of soluble calcium salts.

7. A solution of calcium caseinate which contains only two equivalents of base for each molecule of casein is curdled by rennin:

$$\underset{\text{Soluble}}{\text{Casein Ca}} \xrightarrow{\text{enzyme}} \underset{\text{Insoluble}}{(\text{paracasein})_2\text{Ca}}$$

8. A solution of casein neutral or acid to phenophthalein which will not curdle on the addition of rennin can be made to curdle by the addition of rennin if an amount of a soluble calcium salt, insufficient in itself to cause the precipitation of the casein, is added to the casein solution previous to the addition of rennin.

This curdling is due to one or two causes, as the case may be: First, by an interchange of bases, the sodium, potassium or ammonium caseinates originally in the solution are changed to calcium caseinates and these by the action of the rennin are changed to paracaseinates. Second, the excess calcium salt added to the solution causes a repression in the dissociation of the calcium paracaseinate which results in a precipitation or curdling.

9. A solution of calcium caseinate which would curdle on the addition of rennin can be prevented from curdling by the addition of a sufficient amount of a soluble salt of either sodium, potassium or ammonium. The addition of salts of these bases results in a double decomposition whereby the calcium caseinate is changed to a caseinate of the base added. These are converted to paracaseinates by rennin, but owing to the fact that all the paracaseinates of these bases are soluble, no coagulation or precipitation results.

The changes produced by the addition of salts, as outlined in the two preceding paragraphs, are due to double decomposition and may be represented as follows:

$$\text{Casein } Ca_4 + \text{Rennin} = 2\ (\text{Paracasein } Ca_2)$$

Soluble in absence of calcium salts

$$\text{Casein } Ca_4 + \text{Rennin} + CaCl_2 = 2\ (\text{Paracasein } Ca_2) + CaCl_2$$

Insoluble in the presence of calcium salts

$$\text{Casein } Ca_4 + \text{Rennin} + X\ (Na_2CO_3) = 2\ (\text{Paracasein } Na_4) + 4\ (CaCO_3) + (X - 4)\ Na_2CO_3$$

soluble in absence of calcium salts

$$\text{Casein } Ca_4 + CaCl_2 + \text{Rennin} + X\ (Na_2CO_3 = 2\ (\text{Paracasin } Na_4) + 2\ NaCl + 5\ (CaCO_3) + (X - 5)\ Na_2CO_3$$

soluble in the absence of calcium salts.

The Coagulation of Casein Solutions.—It will be seen, therefore, that the coagulation of solutions of casein by rennin involves two distinct processes as follows:

First: the enzyme acts on the soluble casein changing it to paracasein. This action takes place under a wide variety of conditions and may or may not be followed by coagulation depending on the chemical condition of the casein solution.

Second: the paracasein coagulates or forms a curd if the solution is slightly acid in reaction and contains a sufficient amount of soluble calcium salts.

The reason a curd forms under these conditions we believe to be as follows: In the original solution (or milk) the calcium caseinate is dissociated to an extent sufficient to hold it in colloidal solution, but on the addition of rennin, two molecules of paracasein are formed from every molecule of casein, and in order that these additional molecules may remain in solution it is necessary that some of them become dissociated. The presence of soluble calcium salts represses or inhibits this additional dissociation and results in a slow precipitation with the formation of a curd which mechanically carries down with it other substances present, i.e., in milk, the fat and some of the salts. especially the dicalcium phosphate.

The Changes Produced by the Addition of Rennin to Milk.—Perfectly fresh cow's milk which has not aged or developed acidity will not curdle on the addition of rennin. If such milk is allowed to

TABLE 4.—BASES PRESENT IN HUMAN MILK AND COW'S MILK

	Human Milk		Cow's Milk	
	In 100 C.c. Original Milk	In 100 C.c. Serum	In 100 C.c. Original Milk	In 100 C.c. Serum
Calcium	0.0354	0.0214	0.144	0.048
Magnesium	0.0030	0.0030	0.013	0.007
Sodium	0.0147	0.0147	0.055	0.055
Potassium	0.0711	0.0711	0.120	0.120

age or develop acidity, it will curdle after the addition of rennin, the nature of the curd being wholly dependent on the acidity of the milk. The proper control of the consistency of the curd formed in milk is an important factor entering into the manufacture of the different forms of cheese and is regulated by the degree of acidity allowed to develop in the milk and cheese during the cheese making process.

Perfectly fresh breast milk will not curdle on the addition of rennin, but if the milk has been allowed to develop acidity, a very small amount of a very finely divided precipitate may be produced.

As the degree of acidity and the amounts and nature of the bases present have a marked influence on the nature of the curd produced by the action of rennin, it will be seen that the salts present in the serum of milks will influence the nature of the curd produced by the action of rennin in milk. In this connection the figures in Table 4 will show the amounts of the different bases present in the two milks under consideration.

Especial attention is called to the relations between the amounts of calcium and the sum of sodium and potassium in the two milks. It has been calculated from the above figures that in the case of human

milk there are 7.2 gm. equivalents of calcium for each 10 gm. equivalents of sodium and potassium, while in cow's milk there are 13.2 gm. equivalents of calcium for each 10 gm. equivalents of sodium and potassium. Stating this in another way, we may say that in human milk there are 3.6 atoms of calcium present for each 10 atoms of sodium and potassium, and in cow's milk there are 6.6 atoms of calcium present for each 10 atoms of sodium and potassium.

This difference in the two milks between their relative content of calcium, the curd promoting element and sodium and potassium, the curd retarding elements, is sufficient to explain all the differences noticed in the effect produced by rennin in the two milks.

If this relation between the calcium and the sodium and potassium content of cow's milk is readjusted by the addition of sodium citrate, cow's milk will react like human milk upon the addition of rennin.[6]

TABLE 5.—Showing Action of Increased Acidity of Milk on Calcium Salts and on Curdling Time by Rennin. Milk Maintained at Body Temperature During the Experiment

Age in Hours	Acidity of 100 C.c. as N/10	Insoluble CaO in 100 C.c.			Soluble CaO in 100 C.c., Gm.	Insoluble Inorganic P_2O_5 in 100 C.c. ($CaHPO_4$) Gm.	Soluble Inorganic P_2O_5 in 100 C.c. Gm.	C.c. Rennin Added per 100 C.c. Milk	Coagulation Time
		Total Gm.	As $CaHPO_4$ Gm.	As Caseinate. Gm.					
	10.0	0.1144	0.0515	0.0629	0.0427	0.0399	0.0429	1	1 hr. 10 min.
4	12.0	0.1102	0.0470	0.0632	0.0469	0.0364	0.0464	1	18 min.
5	14.0	0.1090	0.0457	0.0633	0.0481	0.0354	0.0474	1	6 min. 5 sec.
6	15.6	0.1041	0.0431	0.0610	0.0530	0.0334	0.0494	1	2 min.
7	19.6	0.0974	0.0418	0.0556	0.0597	0.0324	0.0504	1	1 min. 10 sec.
8	21.0	0.0922	0.0374	0.0548	0.0649	0.0290	0.0538	1	50 sec.
9	29.0	0.0775	0.0319	0.0456	0.0796	0.0247	0.0581	1	18 sec.
10	33.0	0.648	0.0255	0.0393	0.0923	0.0198	0.0630	1	Immediate

The Influence of the Acidity of Milk on the Action Produced by Rennin in Such Milk.—If by the action of the common lactic acid producing organisms, fresh cow's milk is allowed to develop a degree of acidity insufficient in amount to produce curdling of the milk it will be found that (1) the curdling time after the addition of rennin will decrease with the increase in acidity. (2) The soluble calcium in the milk will increase with the increase of acidity. This is due to the splitting off of calcium from the calcium caseinate and the action of the acid on the insoluble calcium phosphate in the milk. (3) The curds formed by the addition of rennin will show progressive increase in toughness with the increased development of acidity. The curds from the more acid milks will be extremely tough and prone to coalesce into firm compact masses, while the curds from the less acid milks will be very soft and very easily broken up. This change in the nature of the curd with the increase of acidity is due to the action of the lactic

6. Bosworth, A. W., and Van Slyke, L. L.: Am. J. Dis. Child. **7**:298 (March) 1914.

acid on the calcium of the calcium caseinate, producing calcium lactate and acid calcium caseinate and also changing the insoluble neutral calcium phosphate, which is present in cow's milk and has no influence on rennin action, into soluble acid calcium phosphate and calcium lactate, both of these salts favoring coagulation upon the addition of rennin to the milk. The changes in the calcium compounds brought about by the souring of milk are shown in Table 5.

As soluble calcium salts favor curd formation and as the increase in the acidity of milk due to souring increases the amount of soluble calcium in the milk, it will be seen that the prevention or retardation of the action of the bacteria responsible for the souring of milk is a very important factor to be considered in the handling of milk to be used for infant feeding. In this connection it should be mentioned that the very best grades of milk, which, when comparatively fresh, will give a soft curd with rennin, will develop sufficient acidity in less than twenty-four hours, if unpasteurized, to give a firm curd with rennin. This fact offers a very strong argument in favor of the pasteurization immediately after milking of all milk intended for infant feeding. Such pasteurization accomplishes two things: (1) a reduction in the number of lactic acid organisms in the milk which will therefore delay the development of acidity; and (2) a change in the calcium which results in an increase in the amount of insoluble calcium and a decrease in the amount of soluble calcium, a condition tending to decrease the toughness of the curds produced by the action of rennin.

CONCLUSIONS

A method for the preparation of pure caseins is given, and it is found that the caseins from cow's milk and human milk are acids having the same chemical composition and the same chemical characteristics, the two caseins forming the same series of salts with bases.

In cow's milk the casein is present as a calcium caseinate, while in human milk the casein is probably present as a potassium caseinate.

When rennin is added to solutions of casein (or to milk) the casein is split into two equal molecules of paracasein.

The addition of rennin to solutions of casein (or to milk) may or may not result in coagulation, depending on the nature of the salts in the solution (or milk).

Coagulation is promoted by soluble calcium salts and is retarded or inhibited by the addition of soluble salts of sodium, potassium, or ammonium.

The development of acidity in cow's milk favors coagulation after the addition of rennin; the greater the acidity the tougher the curds.

Milk, on entering the infant's stomach, is acted on by the enzymes present. The enzyme rennin, acting on casein, changes it to paracasein.

Breast milks contain small amounts of casein and small amounts of soluble calcium with relatively large amounts of sodium and potassium. The action of rennin on breast milks, therefore, results in no curdling or the production of only a very small amount of very finely divided curds.

Breast milk enters the mouth, the stomach and the intestines in a liquid state. It does not form large curds in the stomach, and, therefore, cannot block the pylorus.

Cow's milk, reconstituted cow's milk, or any of its modifications contain large amounts of casein and soluble calcium with relatively small amounts of sodium and potassium. The action of rennin on these milks or their modifications, owing to their high casein and soluble calcium content, results in the production of large flocculent curds which at body temperature may coalesce and form large masses. These masses are a mixture of paracasein, fat and milk salts.

Cow's milk, reconstituted cow's milk, or any of its modifications enter the mouth and stomach as a liquid, but in the stomach part of the milk may be separated into curds by the action of rennin. These curds may become very large, in fact, large enough to prevent their passage through the pylorus, and in some cases the pylorus may become blocked by them. These masses of curds may remain in the stomach for days and each feeding may add to their size.

Fresh cow's milk does not curdle on the addition of rennin. Curd formation depends on the development of acidity in the milk.

All milk used for infant feeding should be pasteurized immediately after milking.

Under no condition should old milk be used for infant feeding, even if it has been pasteurized thoroughly.

The modification of cow's milk, to adapt it to infant feeding, should include some procedure to prevent the curdling of the casein. Such a procedure has been given in a previous paper.

The salts of milk, both on account of their nutritive value and the influence they have on the other food components of milk, demand more consideration than they now receive in infant feeding.

The influence of the salts on the mechanical condition of the milk after it reaches the stomach on the digestibility of the other food components of the milk, on the availability of the food components after digestion and on the utilization of the vitamins of the milk are pertinent questions which the pediatrician of today cannot answer intelligently, and because he cannot answer them, he is quite likely to ignore them.

A discussion of certain phases of the salt content of milk in its relation to infant feeding has been given in a recent paper.[7]

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7. Bosworth, A. W.: Ann. Med. **1**:3, 1921.

VITAL CAPACITY OF THE LUNGS OF CHILDREN *

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The vital capacity of the lungs is the volume of air which can be expelled after the deepest possible inhalation. We have been unable to find any recorded measurements of vital capacity in normal children, and this was one reason for making these determinations. West [2] has shown that vital capacity in adults varies with the surface area more closely than with any other standard tried. It was not our object to determine the truth of this relation in normal children, but it came out in our work. Peabody [1] has demonstrated the importance of the reduction in vital capacity as an index of the tendency to dyspnea in cardiac disease and has emphasized the importance of vital capacity determinations in diagnosis, prognosis and treatment of vital capacity. It is our primary object to confirm, with regard to children, Peabody's observations in adults, but naturally the vital capacity of normal children had first to be determined. We have made a number of measurements in children in the Heart Clinic of the Children's Hospital, and these we shall publish in a later communication.

METHOD USED

We used for all our determinations the Standard spirometer, made by the Narragansett Machine Co., Providence, R. I. With individual sterilized mouthpieces, each child was coached to take the fullest possible inspiration and then to put forth his best effort in making the maximum expiration. No determination was considered satisfactory unless two determinations came within a margin of 20 c.c. Vital capacity is, of course, the maximum expiration, but we felt that each determination should be checked; two measurements differing more than 20 c.c. from one another would be open to the criticism that the higher figure was

* Received for publication, Feb. 22, 1921.

1. Peabody, F. W., and Wentworth, J. A.: Clinical Studies of the Respiration. IV, Arch. Int. Medicine **20**:443 (Oct.) 1917.

2. West, H. F.: Clinical Studies of the Respiration. VI, Arch. Int. Med. **25**:231 (March) 1920.

due to two expirations instead of one expiration, or that the lower figure was due to a poor try. In a number of cases we have determinations in the same children at intervals of a week, repeated at seven or eight successive periods, and these results were practically constant. Proper coaching of the children and experience are of the greatest importance in securing reliable results. Children below seven years do not cooperate well.

SOURCES OF OUR MATERIAL

Boys between 8 and 15 years of age and girls between 7 and 13 years, inclusive, of the class of people who would attend an outpatient clinic, of various nationalities—Syrian, Irish, American, Italian and Jewish—were measured. These measurements were made in the outpatient departments of the Children's Hospital and of the Boston Floating Hospital, at a boys' club, at an orphan asylum, and at two settlement houses. Each child was examined physically to rule out any children with cardiac or pulmonary disease. Each child was weighed stripped, and measured as to height without shoes. The number of children accepted was 413 boys and girls. Of these, sixty-three were excluded on account of inability to cooperate on account of age. There remained 350 cases, 266 boys and eighty-four girls.

We used the revised tables of Wood [3] for our standard for weights and for heights. The weights as given by Wood include indoor clothes, and since our children were all weighed stripped, it was necessary in determining those cases below normal weight for height, to deduct a certain percentage of the total weight to allow for this factor. In the tables published by Dr. J. L. Morse,[4] 7 per cent. of the total weight for boys is allowed for indoor clothes, and 8 per cent. for girls. For convenience, we allowed 7.5 per cent. for both boys and girls. It is held by Emerson and Manny [5] that the zone of health, as allowed for by Wood, that is, the difference between the obese and the malnourished, is too narrow. A more reasonable zone would allow the deduction of 7 per cent. from the average weight, to include children to this extent under weight for height. These could still be considered normal. For convenience we used the factor 7.5 per cent., making a total deduction of 15 per cent. to be made from the figures of Wood. It may be pointed out that 7.5 per cent. is too much to allow as a reduction from the figures of Wood because this would put the lower boundary of the zone of health below that of Emerson and Manny, even though Wood's curve follows very closely that of Boas and Burk, set forward six months by Emerson and Manny and used by them as

3. Wood, T. D.: Right Height and Weight for Boys and for Girls. Child Health Organization.

4. Morse, J. L.: Case Histories in Pediatrics.

5. Emerson, W. R. P., and Manny, F. A.: Weight and Height in Relation to Malnutrition. Arch. Pediat. **37**:468 (Aug.) 1920.

TABLE 1.—Vital Capacity, Weight and Surface Areas of Boys

Height, Inches	Age, Years	Weight, Pounds	Vital Capacity, C.c.	Surface Area, Sq. M.
69.8	15	132	2,220	1.75 DB
67	13	76*	1,300	1.218 †
66.9	13	79.6*	1,260	1.258
66.6	14	138.8	2,220	1.73 DB
65.1	15	115.2*	1,920	1.56 DB
65	15	129	2,200	1.65 DB
64.8	14	119.5	2,260	1.60 DB
64.4	14	110.2	2,100	1.51 DB
63.4	14	125.7	2,180	1.60 DB
63	15	93	1,600	1.40 DB
63	13	121	1,900	1.56 DB
63	13	88*	1,960	1.342
62.9	15	98.6	1,600	1.43 DB
62.7	15	101	1,800	1.44 DB
62.6	14	102.7	1,340	1.44 DB
62.6	12	97	1,680	1.42 DB
62.2	15	90	1,300	1.35 DB
62	15	91	1,400	1.36 DB
61	15	92	1,300	1.35 DB
61	14	102.8	1,800	1.38 DB
61	14	96	1,400	1.39 DB
61	13	103	1,680	1.43 DB
60.5	13	94	1,160	1.37 DB
60.5	13	100	1,120	1.42 DB
60.5	13	94	1,420	1.37 DB
60.5	11	95	720	1.38 DB
60.4	14	101.4	1,380	1.39 DB
60.2	13	100	1,600	1.39 DB
60	13	97	1,380	1.37 DB
60	15	89	1,400	1.32 DB
59.7	14	85.6*	1,400	1.320
59.7	13	87.5	1,160	1.338
59.6	14	108	1,340	1.43 DB
59.4	13	85	1,240	1.313
59.4	13	90	1,480	1.32 DB
59.4	14	86.1	1,560	1.323
59.4	15	88.7	1,000	1.31 DB
59.3	15	93.6*	2,240	1.33 DB
59.2	13	87.5	1,500	1.338
59.2	15	108.5*	1,500	1.43 DB
59	14	75	1,100	1.209
59	13	93	1,320	1.33 DB
59	13	73*	1,520	1.187
59	12	89	1,440	1.31 DB
58.9	14	88.1	1,660	1,345
58.8	15	85.3	900	1.316
58.6	13	87.3	1,500	1.336
58.5	14	88	1,560	1.342
58.5	13	84	1,600	1.302
58.5	13	79.7*	1,400	1.258
58.5	12	77.1*	1,220	1.232
58.4	14	90.1	1,360	1.28 DB
58.3	11	82.7	1,080	1.288
58.1	13	86.5	1,340	1.327
58.1	13	80.7	1,220	1.267
58.1	12	75.5*	1,280	1.213
58	13	79*	1,540	1.251
58	13	96.5	1,360	1.33 DB
58	13	82.9	1,560	1.290
58	13	88	1,580	1.342
58	13	71*	1,120	1.166
57.9	15	95.8*	1,260	1.21 DB
57.8	13	82.5	1,400	1.286
57.7	13	85.5	1,500	1.318
57.6	13	84.9	1,420	1.311
57.6	12	83	1,300	1.293
57.5	14	73.5*	1,020	1.192
57.5	13	78*	1,200	1.239
57.5	12	85.7	1,400	1.320
57.3	14	76.7*	1,360	1.225
57.3	12	70.8*	1,080	1.163
57.2	10	73.4*	1,220	1.192
57.1	13	67.2*	1,140	1.122
57.1	14	81.1	1,260	1.274
57	14	90	1,220	1.27 DB
57	13	95	1,440	1.30 DB
57	13	92	1,340	1.28 DB
57	13	83	1,320	1.293
56.9	14	79.1	1,100	1.254
56.8	13	74.5*	1,020	1.202
56.7	13	71.1*	1,100	1.168
56.5	15	79.5*	1,420	1.256
56.5	14	83.5*	800	1.297
56.5	13	81.2	1,100	1.274
56.5	13	73.8*	1,320	1.197
56.5	12	75*	1,100	1.209
56.5	12	69*	840	1.141
56.4	12	80.4	1,440	1.265
56.1	12	86.5	1,120	1.327

* Denotes those cases falling below 7.5 per cent. normal weight for height.
† All surface areas, except those marked DB, are from Benedict and Talbot. DB denotes Dubois and Dubois.

TABLE 1.—VITAL CAPACITY, WEIGHT AND SURFACE AREAS OF BOYS—(*Continued*)

Height, Inches	Age, Years	Weight, Pounds	Vital Capacity, C.c.	Surface Area, Sq. M.
56.1	11	80.3	1,220	1.263
56	15	82.3	1,280	1.283
56	13	76	1,420	1.218
56	13	75.6	1 080	1.216
56	13	73*	1.200	1.187
56	12	75	1.400	1.209
56	12	73*	1 880	1.187
56	12	76	1,120	1.218
56	12	69*	600	1.141
56	11	71*	1.180	1.166
55.9	11	90	1,220	1.26 DB
55.8	12	80.3	1,100	1.263
55.8	12	66.9*	1.140	1.117
55.8	12	62.7*	1,200	1.070
55.7	13	73.7	1.300	1.195
55.6	12	77.3	1,300	1.232
55.5	13	75.5	1,200	1.213
55.5	11	85.7	1,580	1.320
55.5	10	67.2*	1,080	1.122
55.4	14	76.1	1 046	1.220
55.4	12	65.1*	1 900	1.100
55.4	11	71.5	1 100	1.171
55.4	11	70.2	1.200	1.156
55.3	11	67.5*	1,120	1.124
55.3	11	72	1.440	1.175
55.1	12	73.1	1 140	1.190
55.1	11	77.6	1,240	1.237
55.1	11	70	1.180	1.154
55.1	10	65.6*	1.300	1.105
55	12	69*	1.300	1.141
55	12	65*	1 360	1.098
55	12	66*	1.200	1.107
55	12	67.7*	840	1.126
55	12	74	1,280	1.197
55	12	72.5	1 020	1.180
55	11	74	1.060	1.197
55	11	63*	1,100	1.075
55	11	67.5*	1,120	1.124
55	11	73	1,250	1.187
55	11	70	1.400	1.154
55	10	70	1,140	1.154
54.9	13	76.5	1.200	1.223
54.8	11	68.6*	1.000	1.136
54 8	11	70.8	1.200	1.163
54.7	12	72.3	900	1.178
54.7	12	71.5	1 000	1.171
54.7	10	64.6*	820	1.093
54.7	10	67.5*	1.120	1.124
54.7	9	69.1	1.000	1.144
54.7	11	63.3*	1.240	1.078
54.6	13	68.2*	1 260	1.131
54 5	13	73.5	1.150	1.192
54.5	12	59.1*	1 020	1.032
54.4	12	66.5*	1 040	1.112
54 4	10	67.4	880	1.124
54.2	11	66.6	1.040	1.114
54	12	64*	1.100	1.086
54	12	68.3	1 100	1.131
54	12	72	1,300	1.175
54	12	69	1,120	1.141
54	12	64*	1.160	1.086
54	12	69	1.120	1.141
54	11	75	1.240	1.209
54	11	80	1 300	1.260
54	10	64*	1 080	1.086
54	13	69	1,000	1.141
54	9	68.7	700	1.136
53.8	13	66.7*	1 140	1.114
53.7	12	66*	1 140	1.107
53.7	11	64.4*	1 280	1.090
53.7	13	67*	1.200	1.119
53.6	12	60*	960	1.040
53.5	13	66*	840	1.107
53.5	14	70.3	1 700	1.156
53.5	12	66*	1 200	1.107
53.5	12	67.5	1 200	1.124
53.4	11	66.9	1 000	1.117
53.2	10	69.2	1 140	1.144
53	12	66	1 040	1.107
53	12	68	1 220	1.199
53	12	77	1 000	1.230
53	12	68.6	1.080	1.136
53	12	60*	1 120	1.040
53	11	63*	940	1.075
53	11	80	1.120	1.260
53	11	78	1.260	1.239
53	11	65	1.120	1.098
53	11	63.3*	1,060	1.078

* Denotes those cases falling below 7.5 per cent. normal weight for height.

† All surface areas, except those marked DB, are from Benedict and Talbot. DB denotes Dubois and Dubois.

TABLE 1.—VITAL CAPACITY, WEIGHT AND SURFACE AREAS OF BOYS—(*Continued*)

Height, Inches	Age, Years	Weight, Pounds	Vital Capacity, C.c.	Surface Area, Sq. M.
53	11	68	1,140	1.129
53	10	63	1,000	1.075
52.8	10	70.5	1,260	1.159
52.7	10	68.3	1,100	1.131
52.7	12	58.1	1,160	1.019
52.6	13	68	1,200	1.129
52.6	11	67.9	1,200	1.129
52.5	10	60.5*	800	1.045
52.4	10	66	1,060	1.107
52.4	9	56.5*	1,200	0.988
52.2	13	59.2*	1,140	1.032
52.2	10	66.8	920	1.117
52.1	11	66.5	1,000	1.112
52.1	8	53	900	0.934
52	12	63	620	1.075
52	12	61*	840	1.052
52	12	58*	980	1.016
52	11	58*	1,020	1.016
52	11	59*	920	1.029
52	11	68	1,000	1.129
52	11	70.5	1,100	1.159
52	10	63	1,000	1.075
52	10	63.6	1,000	1.083
52	10	65	1,240	1.098
52	10	62	940	1.062
52	10	77	860	1.230
51.9	9	61	940	1.052
51.8	12	68.1	1,060	1.131
51.8	11	63.6	1,020	1.083
51.7	9	50.4*	1,100	0.903
51.6	9	54.3*	880	0.947
51.6	10	61	820	1.052
51.5	13	61.5*	1,100	1.057
51.4	12	55.6*	1,040	0.973
51.3	12	86	840	1.323
51.1	8	59.8	900	1.040
51	12	66	800	1.107
51	11	58*	1,020	1.016
51	11	51*	1,020	0.911
51	11	61	780	1.052
51	10	57.6*	960	1.014
51	10	56	980	0.978
51	10	60.5	1,100	1.045
51	10	61	660	1.052
51	9	65	1,100	1.098
50.7	11	56.8*	900	0.998
50.6	11	59.5	920	1.035
50.5	11	58*	1,000	1.016
50.5	9	52.2	980	0.924
50.5	9	60	1,000	1.040
50.4	9	58.2	940	1.019
50.3	11	57.4	1,020	1.011
50	12	58.1	750	1.019
50	12	65	1,000	1.098
50	11	72	920	1.175
50	10	62	720	1.062
50	10	57	800	1.003
50	10	59	900	1.029
50	9	55*	1,100	0.968
49.9	11	53.5*	860	0.939
49.8	9	61.8	900	1.062
49.7	11	56.4*	820	0.988
49.4	9	55.2	980	0.963
49.3	8	52.3	800	0.924
49	12	58*	820	1.016
49	11	48*	840	0.871
49	10	50.5*	860	0.903
49	10	58	800	1.016
49	9	54.6	820	0.952
49	8	51.9	820	0.921
48.7	10	49*	800	0.884
48.6	10	55.3	900	0.963
48.5	9	49*	620	0.884
48.5	10	61	1,100	1.062
48.5	10	60.8	720	1.050
48.4	9	57	800	1.003
48.3	8	48.3	600	0.873
48.2	9	52.2*	820	0.924
48.1	10	51.1	680	0.913
48	10	47*	720	0.860
47.6	8	45.3*	800	0.839
47.5	8	53*	760	0.934
47.2	8	46.6*	540	0.855
47	10	48.5*	800	0.876
46.7	8	48	640	0.871
46.7	8	46.1*	820	0.850
46.7	8	52.1	620	0.924
46.2	9	50.7	820	0.906
46.1	8	49	720	0.884

* Denotes those cases falling below 7.5 per cent. normal weight for height.

† All surface areas, except those marked DB, are from Benedict and Talbot. DB denotes Dubois and Dubois.

TABLE 2.—Weight, Vital Capacity and Surface Area of Girls

Height, Inches	Age, Years	Weight, Pounds	Vital Capacity, C.c.	Surface Area, Sq. M.
59.5	13	97.3*	1,380	1.37 DB
59.3	12	99	1,300	1.37 DB
59	13	83*	1,280	1.248†
59	12	74.8*	960	1.158
58.8	12	92	1,320	1.32 DB
58.8	11	83	1,300	1.248
58.3	12	90.3	1,320	1.29 DB
58	13	88	1,220	1.295
58	13	100.5	1,000	1.37 DB
57.8	12	82	1,360	1.237
57.8	10	80.5	1,160	1.221
57.5	12	86	1,040	1.277
57	13	79.5	1,240	1.212
57	13	79	1,100	1.207
57	13	98	1,100	1.3 DB
57	11	81.5	1,240	1.233
57	7	46.5*	840	0.845
56.5	12	75*	1,280	1.166
56.5	11	76	1,180	1.176
56.3	9	76.5	980	1.178
56	11	73.6	980	1.153
56	10	48.3*	1,000	0.866
55	12	71	980	1.125
55	12	68*	920	1.090
55	10	62*	920	1.026
55	9	68.5	1,080	1.095
54.8	10	85	1,120	1.268
54	13	69.5	1,200	1.107
53.5	12	67.5	1,000	1.085
53.5	12	61*	1,000	1.016
53.5	11	66	780	1.069
53.3	10	61.5	1,000	1.021
53.3	9	61.5	980	1.021
53	12	66.8	740	1.078
52.5	7	59.5*	900	0.999
52.5	12	60.3*	1,120	1.006
52	13	70*	920	1.114
52	12	70.5	840	1.119
52	11	67.5	1,040	1.085
51.8	10	63	860	1.088
51	9	70	920	1.114
51	9	54*	800	0.936
50.5	12	56*	940	0.959
50	11	57	840	0.971
50	11	62	920	1.026
50	11	50*	740	0.890
50	10	60.5	720	1.009
50	10	58.5	740	0.986
50	10	57.5	860	0.976
50	9	51*	840	0.903
49.5	10	53*	560	0.926
49.1	9	50*	720	0.890
49	11	83.3	1,180	1.25
49	10	50*	700	0.890
49	10	57	840	0.971
49	9	55.5	760	0.954
49	8	47.5*	540	0.858
48.5	7	46.3	690	0.840
48.3	10	52.3	700	0.916
48.3	9	48.5*	940	0.869
48	10	58.3	720	0.984
48	10	48*	740	0.863
48	8	47.6*	540	0.861
48	7	46	480	0.835
48	7	56.3	660	0.961
47.8	8	50	500	0.890
47.5	10	55.3	640	0.951
47.5	7	43.5	820	0.787
47	9	53	420	0.926
47	9	50	540	0.890
46.5	7	45.3	760	0.820
46	8	50.5	960	0.895
46	8	51	760	0.903
46	7	47	740	0.853
46	7	48	640	0.863
45.8	8	48	760	0.863
45	8	52	720	0.913
44.8	8	47.5	700	0.858
44.5	8	52	600	0.913
44	7	43	680	0.782
44	7	43	500	0.782
43.5	7	46.3	540	0.840
43.3	7	46.3	660	0.840
43	7	42.5	680	0.774

* Denotes those cases falling below 7.5 per cent. normal weight for height.
† All surface areas, except those marked DB, are from Benedict and Talbot. DB denotes Dubois and Dubois.

their basis. As it happened, the vital capacity of normal children and of children below normal weight for height differed very little. Those cases falling below 7.5 per cent. weight for height are marked with an asterisk.

TABLE 3.—VITAL CAPACITY OF LUNGS FOR BOYS

Group	Number Studied	Height, Inches	Average Vital Capacity, C.c.	Surface Area, Square Meters	Number Within 20% of Normal Vital Capacity	Number Falling Below 80% Average Vital Capacity	Highest Vital Capacity	Lowest Vital Capacity
I	8	63–69.8	2,080	1.600	7	1	2,220	1,600
	4*		1,610	1.344	4	0	1,960	1,260
Total	12							
Average	...	.....	1,845	1.514				
II	50	57–63	1.390	1.338	46	4	1,800	720
	16*		1 343	1.233	15	1	2,240	1,020
Total	66							
Average	...	.....	1,366	1.313				
III	87	51–57	1.100	1.157	79	8	1,580	620
	57*		1.091	1.093	49	8	1,420	600
Total	144							
Average	...	.....	1,095	1.132				
IV	27	46–51	840	0.988	24	3	1,100	600
	17*		814	0.917	15	2	1,100	540
Total	44							
Average	...	.....	827	0.961				

* Denotes those cases falling below 7.5 per cent. normal weight for height.

TABLE 4.—VITAL CAPACITY OF LUNGS FOR GIRLS

Group	Number Studied	Height, Inches	Average Vital Capacity, C.c.	Surface Area, Square Meters	Number Within 20% of Normal Vital Capacity	Number Falling Below 80% Average Vital Capacity	Highest Vital Capacity	Lowest Vital Capacity
I	26	59.5–53	1,120	1.204	24	2	1.380	740
	8*		1,025	1.052	8	0	1,280	840
Total	34							
Average	...	.....	1,072	1.168				
II	22	53–47	759	0.976	18	4	1,180	420
	14*		786	0.900	11	3	1,120	540
Total	36							
Average	...	.....	773	0.938				
III	14	47–43	693	0.849	12	2	960	500

* Denotes those cases falling below 7.5 per cent. normal weight for height.

The tables used for surface area are the work of Benedict and Talbot [6] who kindly allowed us to use these tables before publication.[7] For the heavier children we used the chart of Dubois and Dubois.[8]

6. Talbot, F., and Benedict, F. G.: The Metabolism and Growth from Birth to Puberty, Carnegie Institution, Washington; Publication 302.

7. These figures are available now in Carnegie Publication No. 302.

8. Dubois, D., and Dubois, E. F.: Arch. Int. Med. **17**:863 (June) 1916.

Our readings of the vital capacity for boys and girls are shown in Tables 1 and 2. These readings were divided into four groups for boys and three groups for girls (Tables 3 and 4). The difference in the height between the shortest and tallest children in the case of boys was 23.8 inches and of the girls 16.5 inches. Accordingly, we allowed six inches roughly for each group. It will be noticed that the first group for boys is a little over six inches and the last group for boys is a little under six inches. The third group of girls is from 43 to 47.1 inches, a division made necessary by the small number of girls of the shortest height.

In each group the average vital capacity is given first for children of normal height and weight. Below this figure the vital capacity is given for those falling below 7.5 per cent. of the average weight for height.

The next column is the average surface area for each group. The figures for surface area are given in square meters and those for vital capacity in cubic centimeters. In order to compare the two, the vital capacity can be read in litres.

TABLE 5.—Summary and Ratio of Vital Capacity to Surface Area

	Average Vital Capacity, Liters (A)	Surface Area, Square Meters (B)	Ratio: Vital Capacity to Surface Area (A ÷ B)
Boys:			
Group I	1.8	1.5	1.2
Group II	1.4	1.3	1.1
Group III	1.1	1.1	1.0
Group IV	0.8	1.0	0.8
Girls:			
Group I	1.1	1.2	0.9
Group II	0.8	0.9	0.7
Group III	0.7	0.9	0.6

For the second group of boys, which contained next to the largest number, the vital capacity in liters would be 1.4, and the surface area 1.3 square meters. For the third group, which contained the largest number of boys, the vital capacity in liters was 1.1, and the surface area 1.1 square meters. These two groups show very markedly the close relationship between vital capacity and surface area. Even in the first group with comparatively few determinations the vital capacity was 1.8 liters and the surface area 1.5 square meters.

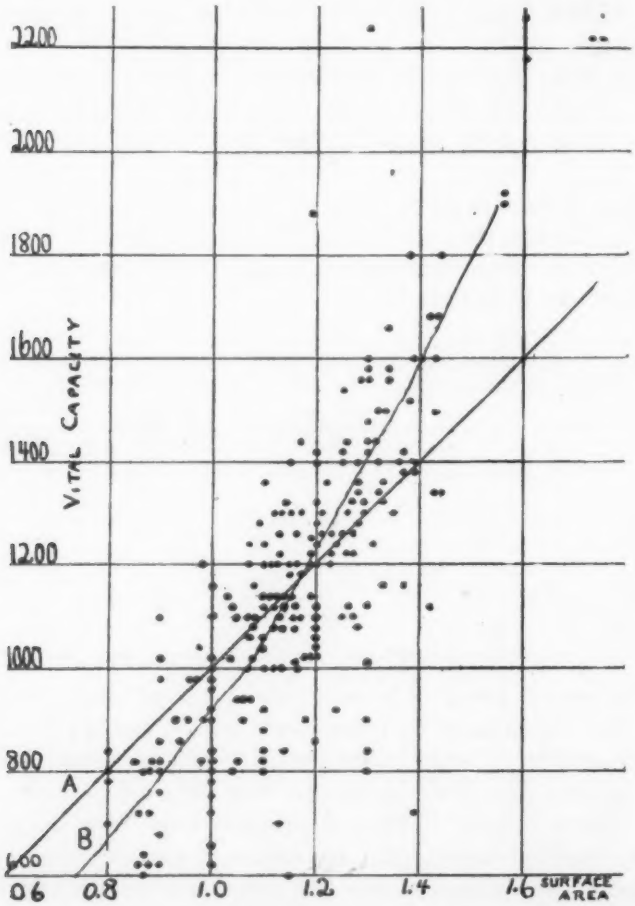
The next column in the tables gives the number of cases in which the vital capacity fell below 20 per cent. of the average for this group: a variation of 10 per cent. in adults is considered normal. Children, as a rule, are more difficult to handle and are usually harder to make cooperate, so that they vary more from the average than adults. A variation of 20 per cent. includes most of the cases.

The next column in the tables gives the number of cases in which vital capacity fell below 20 per cent. of the average for this group.

The next column gives the number below 80 per cent. of the average; not 80 per cent. below, but below 80 per cent. of the average.

In pathologic conditions there is a fall in vital capacity. From our determinations the fall should amount to more than 20 per cent. of the average to be considered significant.

The highest and lowest vital capacity is given for each group. This shows a wide variation of about 20 per cent. from the average.



A.—When vital capacity and surface area are identical theoretically.
B.—Experimental Curve.

Group 1 of the girls gave an average vital capacity of 1.1 liters and a surface area of 1.2 square meters. Group II of the girls gave an average vital capacity of 0.8 liters and a surface area of 0.9 square meters.

In Table 5 we have summarized the vital capacity in liters, the surface area in square meters, and the ratio of vital capacity to surface

area for each group—first of boys, then of girls. Group I of our girls, our best group of girls, showed a vital capacity of 1 liter to 0.9 of a square meter of surface area; and our best group of boys, Group III, showed a vital capacity of 1 liter to 1 square meter of surface area.

Although the normal children and those falling below 7.5 per cent. of normal were considered separately, the vital capacity showed very little variation; in fact, they corresponded very closely, except in the first group of boys, which was a very small one.

On a graph, a line was drawn arbitrarily to make the vital capacity and surface area correspond exactly. We then plotted our actual figures and found that they came very close to this arbitrary line.

CONCLUSIONS

1. A very close relationship was found between vital capacity and surface area in children.

2. There is practically no difference between children considered in the tables for normal weight for height and those falling 7.5 per cent. below the normal.

3. The determinations of vital capacity for girls were on the whole much lower than those for boys, but the same relation held between vital capacity and surface area.

4. Determinations of vital capacity below seven years of age are unreliable.

THE FRAGILITY OF THE RED BLOOD CORPUSCLES IN INFECTIOUS DISEASES *

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The study of the fragility of the red blood cells has so far revealed little of interest or importance, aside from the striking decrease in resistance seen in cases of hemolytic family jaundice. Butler [1] in a careful study of red cell fragility investigated among other diseases the resistance of the red blood cells in pneumonia, sepsis, and to a limited extent, scarlet fever and erysipelas. In looking over his results in cases of pneumonia and sepsis, we were impressed by the fact that certain of the severer cases, especially those with a high fever, showed an increased resistance of the red corpuscles. This might be explained in two ways, either there was some chemical or physical change in the blood corpuscles produced by the fever, or else the toxins formed by the infecting agents produced some effect on the red blood cells. We therefore became interested in ascertaining the fragility of the red blood cells in the various infectious diseases and likewise the effect of fever on the red cell resistance.

As many of the infectious diseases are of unknown etiology, it was hoped that, perhaps, something of diagnostic or prognostic importance might result from this investigation. Our material comprises cases from the Contagious Hospital and other cases with infections or high fever. Unfortunately, we were limited in our work by the fact that we were unable to obtain blood from certain contagious conditions; however, we have enough cases from most of the contagious diseases to enable us to draw some conclusions from this work.

METHOD

Three c.c. of blood is withdrawn with a dry Luer syringe into a centrifuge tube containing 3 c.c. of a 0.85 per cent. solution of sodium chlorid and sodium citrate, respectively. The blood is centrifuged until 3 c.c. of clear supernatent fluid can be withdrawn and discarded. The volume of the red blood cells is now in the same proportion as in the original blood. The blood cells and citrated plasma are well mixed and 0.1 c.c. of blood is added to each of a series of ten test tubes containing 1 c.c. of saline solution, beginning at 0.5 per cent. and diminishing in gradations of 0.025 per cent down to 0.275 per cent. After

* Received for publication, March 12, 1921.

* From the Department of Pediatrics and Infectious Diseases, University of Michigan Hospital.

1. Butler: Quart. J. M. **6**:145, 1912.

standing one hour, the test tubes are gently centrifugated and the point of beginning and complete hemolysis is noted. Using this method, normal bloods show a beginning hemolysis at 0.425 per cent. and complete hemolysis at 0.325 per cent. About 5 per cent. of normal bloods show beginning hemolysis at 0.4 per cent.

This method is particularly well adapted to the securing of blood from contagious cases in which a technic using untreated blood is impracticable. Butler has shown that the fragility of the red cells is the same when untreated as in citrated plasma. This we have found to be true. In two cases of hemophilia, our results with untreated blood and citrated blood were exactly the same. The collecting of the blood in citrated saline solution is a great convenience and this method has proved so satisfactory that we have used it in our other studies on red cell fragility.

DIPHTHERIA

In Table 1 are given the results of the fragility tests in diphtheria. There are no striking changes in either the beginning or the complete hemolysis. No difference was noted in the results whether the blood sample was taken before or after receiving the antitoxin. The case of DeGrand is of particular interest. Blood was taken on the first day of the disease before antitoxin was administered, also at the height of a reaction from intravenous administration of antitoxin when the axillary temperature was 107.2 F., and on the sixth day after the patient had recovered and the temperature was normal. The results of the fragility test were exactly the same. There is no hemolytic action of the diphtheria toxin on the red cells. This we have also found to be true in experiments with diphtheria toxin in vitro. The fragility test gives no information in diphtheria.

ERYSIPELAS

Our results in cases of erysipelas show very little deviation from the normal. There is a slight tendency for an increased resistance, and in one rather severe case (Westlock) the resistance is distinctly increased. In the milder cases, and as recovery takes place, the fragility is normal.

Butler found a normal fragility in one mild case of erysipelas. Dudgeon [2] records one case of erysipelas in which there was marked increase in fragility. We have not encountered this phenomenon in any of our cases.

SCARLET FEVER

In this disease we have several patients with increased resistance. This is especially true of the severer cases and in those in which the blood was taken early in the disease. Of especial interest are the cases

2. Dudgeon: Proc. Roy. Soc. Lond., Ser. B. **81**:207, 1909.

TABLE 1.—FRAGILITY OF RED BLOOD CELLS IN DIPHTHERIA

Name	Day of Disease	Temperature	Condition	Beginning Hemolysis	Complete Hemolysis	Remarks
Taxai.....	1	99.8	Good	0.400	0.300	Has been receiving arsphenamin treatments for syphilis
DeGrand.....	1	101.4	Good	0.450	0.325	Before antitoxin
DeGrand.....	1	107.2 ax.	Poor	0.450	0.325	Received 10,000 units diphtheria antitoxin intravenously 30 minutes before—having chills
DeGrand.....	6	98.6	Good	0.450	0.325	Membrane gone
Anderson....	1	103.4	Good	0.450	0.325	
Anderson....	6	98.6	Good	0.450	0.325	Received 20,000 units antitoxin on first day
Reid.....	1	102.8	Good	0.400	0.325	Received 10,000 units antitoxin (after blood was drawn)
Reid.....	5	99.8	Good	0.425	0.325	
Moore.....	2	102.0	Good	0.425	0.325	20,000 units antitoxin (after blood was drawn)
Moore.....	7	98.6	Good	0.425	0.325	
Borden.....	1	103.8	Good	0.400	0.325	10,000 units antitoxin (after blood was drawn)
Borden.....	7	98.6	Good	0.425	0.325	

TABLE 2.—FRAGILITY OF THE RED BLOOD CELLS IN ERYSIPELAS

Name	Day of Disease	Temperature	Condition	Beginning Hemolysis	Complete Hemolysis	Remarks
Schultz.....	2	103.0	Good	0.400	0.325	
Holmstead...	2	99.2	Fair	0.425	0.325	Carcinoma of face
Ulms.....	1	99.4	Good	0.425	0.325	
Westlock.....	3	102.4	Good	0.400	0.275	Temperature 104, night before
Jackson.....	4	98.8	Good	0.425	0.325	Temperature 102, first day
Berger.....	4	99.0	Good	0.400	0.300	Temperature 105, 2 days before

TABLE 3.—FRAGILITY OF THE RED BLOOD CELLS IN SCARLET FEVER

Name	Day of Disease	Temperature	Condition	Beginning Hemolysis	Complete Hemolysis	Remarks
Buffman.....	5	104.4	Poor, toxic	0.375	? not complete at 0.275	Received two Pasteur injections for rabies
Buffman.....	13	101.0	Worse	0.425	0.275	Two blood cultures negative; death from nephritis
Shanklind....	2	102.2	Good	0.425	0.300	
Barker.....	3	102.4	Good	0.425	0.300	Postoperative hernia
Martin.....	4	98.8	Good	0.400	0.275	
Martin.....	6	98.8	Good	0.425	0.350	
Spring.....	8	98.8	Good	0.425	0.325	
Olsen.....	2	98.8	Good	0.450	0.325	
Olsen.....	5	98.8	Good	0.425	0.325	
Travers.....	5	101.0	Poor	0.350	0.275	Bronchopneumonia
Travers.....	33	98.6	Good	0.425	0.325	
Landy.....	4	100.0	Good	0.425	0.325	

of Buffman and Travis. The first mentioned case was fatal, with many complications, including a terminal nephritis. The second was a patient with marked toxemia and a complicating bronchopneumonia. In both patients' blood there was a distinct increase in the red cell resistance. Butler found increased resistance in two out of five cases of scarlet fever. The other patients showed normal fragility. He does not give the temperature record nor the severity of the cases. Teisser and Benard [3] state that the fragility in scarlet fever is normal, unless jaundice is a complication. We had no patients showing complicating jaundice.

TABLE 4.—FRAGILITY OF THE RED BLOOD CELLS IN VARIOLA

Name	Day of Disease	Temperature	Condition	Beginning Hemolysis	Complete Hemolysis	Remarks
Klatt.....	3	104.2	Toxic	0.425	0.325	Severe headache; pains in back; one day before eruption
Mack.....	7	98.6	Good	0.425	0.325	
Barnes.....	6	98.6	Good	0.425	0.325	
Theuerkauf..	6	98.6	Good	0.400	0.325	
Erickson.....	5	98.6	Good	0.425	0.350	

TABLE 5.—FRAGILITY OF THE RED BLOOD CELLS IN VARICELLA

Name	Day of Disease	Temperature	Condition	Beginning Hemolysis	Complete Hemolysis	Remarks
Mansfield....	2	98.6	Good	0.400	0.325	
Visi.....	1	99.8	Good	0.425	0.325	
Cruse.....	10	98.6	Good	0.425	0.350	
Hawks.....	7	98.6	Good	0.425	0.325	

VARIOLA AND VARICELLA

In Tables 4 and 5 are given the results of the fragility tests in variola and varicella. They show nothing of importance, all being within normal limits. Klatt (Table 4) was tested on the third day of the disease, a few hours before the eruption appeared and the temperature dropped. His temperature was 104 F. at the time the blood was taken and his blood showed normal fragility.

MISCELLANEOUS CASES

In Table 6 is shown the fragility test in various conditions. In one case of measles, the fragility was normal. It is to be regretted that more cases were not studied, but we had no material during the period of this investigation. In congenital syphilis the fragility is normal. In a fatal case of polio-encephalitis there was an increase in the resistance. In a fatal case of staphylococcus septicemia there was a distinct

3. Teisser and Benard: Presse med., 1910 (Quoted by Butler).

decrease in fragility. In a case of serum disease (the patient previously having recovered from an attack of meningococcus meningitis), the fragility was normal in spite of a temperature of 105 F.

EFFECT OF FEVER ON FRAGILITY

We have tabulated a number of patients showing fever with reference to its height. It is clearly shown that fever per se is not the important factor in causing an increased resistance of the red blood

TABLE 6.—FRAGILITY OF THE RED BLOOD CELLS IN MISCELLANEOUS INFECTIOUS DISEASES

Name	Disease	Temperature	Condition	Beginning Hemolysis	Complete Hemolysis	Remarks
Bently	Measles	100.0	Good	0.425	0.325	Temperature 104, 2 days before
Haney	Congenital syphilis	98.6	Good	0.425	0.325	Before receiving neoarsphenamin
Lawson	Congenital syphilis	98.6	Good	0.400	0.325	Receiving neoarsphenamin
Lehman	Congenital syphilis	98.6	Good	0.425	0.350	Receiving neoarsphenamin
Mastic	Polio-encephalitis	101.2	Poor	0.425	0.300	Eighth day of disease
Mastic	Polio-encephalitis	102.4	Poor, fatal case	0.400	0.300	Complicating pneumonia twelfth day of disease
Kubin	Staphylococcus septicemia	103.6	Poor, fatal case	0.375	0.275	Delirious; died next day
Blackmoore	Cerebrospinal meningitis	105.0	Good	0.400	0.325	Temperature due to serum reaction; spinal fluid normal

TABLE 7.—EFFECT OF FEVER ON THE FRAGILITY TEST

Name	Temperature	Beginning Hemolysis	Complete Hemolysis	Fragility	Remarks
DeGrand	107.2 ax.	0.450	0.325	Increased	Antitoxin reaction
Blackmoore	105.0	0.400	0.325	Normal	Serum disease
Klatt	104.4	0.425	0.325	Normal	Delirious
Buffman	104.4	0.375	0.275	Decreased	Death
Borden	103.8	0.400	0.325	Normal	
Kubin	103.6	0.375	0.275	Decreased	Death
Anderson	103.4	0.450	0.325	Increased	
Schultz	103.0	0.400	0.325	Normal	
Reid	102.8	0.400	0.325	Normal	
Westlock	102.4	0.400	0.275	Decreased	Severe case
Mastic	102.4	0.400	0.300	Decreased	Death
Barker	102.4	0.425	0.300	Decreased	
Moore	102.0	0.425	0.325	Normal	
DeGrand	101.4	0.450	0.325	Increased	
Mastic	101.2	0.425	0.300	Decreased	
Buffman	101.0	0.425	0.275	Decreased	
Travers	101.0	0.350	0.275	Decreased	Severe case

cells. In looking over our results we are impressed by the fact that the cases which showed a distinct increase in resistance were those in which the disease process was grave and the prognosis serious. In our limited number of cases we are led to the conclusion that a marked increase in the resistance of the red blood corpuscles in an infectious disease is of grave prognosis. The only case with a markedly increased resistance that ended in recovery (a severe toxic case of scarlet fever

with bronchopneumonia), recovery was due to the remarkable influence of intramuscular injections of convalescent blood. An unfavorable prognosis was given before the blood was injected.

If the increased resistance, which was observed only in the most serious cases, is not due to the effect of the fever on the red blood cells, it may be due to the toxins of the invading organisms. It is conceivable that a compensatory mechanism causes the red corpuscles to protect themselves against an injurious toxin by an increase in their resistance to hemolytic agents. However, in diphtheria, we find no increase in resistance, nor was the resistance increased when the red blood cells were allowed to come in contact with diphtheria toxin. Certain organisms are known to produce hemolysins, especially the streptococcus, accordingly an increased resistance may be a defense reaction against certain organisms whose toxins have an especial affinity for the red corpuscles.

CONCLUSIONS

1. No distinctive reaction to the fragility test was found in any of the infectious diseases studied, accordingly the fragility test has no diagnostic value.

2. Fever per se has no effect on the fragility of the red cells.

3. In certain cases of infectious diseases one may find a distinct increased resistance. These cases are usually of great severity and the prognosis is grave.

A RAPID CLINICAL METHOD FOR THE DETERMINATION OF THE REDUCING SUBSTANCE IN THE CEREBROSPINAL FLUID: THE METHYLENE BLUE METHOD*

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It was first stated by Deschambs and Bussy (1852) that the reducing substance is usually found in the cerebrospinal fluid. Since that time numerous articles have appeared on this subject, and recent investigations have proved definitely that the reducing substance is glucose, and that it is always present in the spinal fluid in normal conditions.

At the present time, the methods most generally used in clinical laboratories for the determination of the glucose in the cerebrospinal fluid are those of Haines, Benedict and Lewis and Bang. The Haines method is employed simply for the qualitative determination of the glucose. For the quantitation of the glucose in the spinal fluid, the Benedict and Lewis method and the Bang micromethod give good results. Most American workers have employed the Benedict and Lewis method, or some modifications of it. Employing this method, Schloss and Schroeder[1] found that the glucose content in normal spinal fluid varied between 0.054 and 0.134 per cent. Suzuki[2] recently examined the normal cerebrospinal fluid of children for its glucose content, employing the Bang micro-method. He found that the glucose content in normal fluid varied between 0.055 and 0.067 per cent. Borberg,[3] using the micromethod of Bang, found the glucose content in normal fluid to be about 0.06 per cent., varying from 0.05 to 0.075 per cent. These methods, however, except that of Haines, are complicated by various pitfalls, which render the obtaining of accurate results unduly difficult, especially in the clinical laboratory.

It is well known that the methylene blue solution becomes colorless when it is reduced in the alkaline solution. So far as we have ascertained, no qualitative and quantitative determinations of the glucose in the cerebrospinal fluid have been made with the methylene blue solution. Our methylene blue method for the determination of glucose in the spinal fluid depends on the fact that when the glucose solution

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* From the Department of Pediatrics of the Kyoto Imperial University.
1. Schloss and Schroeder: Am. J. Dis. Child. **11**:1 (Jan.) 1916.
2. Suzuki, T.: Tokyo Tgakukai Zashi (Japanese) **13**:1, 1916.
3. Borberg: Ztschr. f. d. ges. Neurol. u. Psych. **32**:4/5 H., 1916.

is heated with the methylene blue solution in the presence of an alkali, a definite reaction takes place, and the depth of the color is directly proportional to the quantity of glucose present.

The work described in this paper was planned to determine the glucose in the cerebrospinal fluid by the methylene blue method, which we believe contributes to the simplicity and rapidity of the test, without impairing its accuracy.

THE QUALITATIVE TEST

The procedure of the methylene blue method for the qualitative determination of the glucose in the spinal fluid is as follows: Two-tenths c.c. of cerebrospinal fluid is drawn up with a graduated pipet into the test tube. One c.c. of 0.004 per cent. methylene blue solution (Methylenblau f. Bac. Gruebler) is added to the fluid, and then three drops of 10 per cent. potassium hydroxid solution are poured into it. This mixture is heated and boiled for a few seconds. If it contains 0.05 per cent. or more of glucose, the mixture will become colorless. In the absence of glucose in the fluid, the blue color remains unchanged. If it contains less than 0.05 per cent. glucose, the depth of the color varies, strictly depending on the quantity of this substance present. To determine a greater or less amount of the glucose in the spinal fluid, the procedure is repeated for the clinical work in the following manner.

(1) Two-tenths c.c. of the cerebrospinal fluid is transfered to a test tube. To this fluid are added 1.0 c.c. of 0.004 per cent. methylene blue solution and three drops of 10 per cent. potassium hydroxid solution. This mixture is then heated and boiled for a few seconds. If the fluid contains 0.05 per cent. or more of glucose, the mixture becomes colorless.

(2) To 0.14 c.c. of the cerebrospinal fluid are added 1.0 c.c. of 0.004 per cent. methylene blue solution and three drops of 10 per cent. potassium hydroxid solution. It is then heated and boiled for a few seconds. If the fluid contains 0.07 per cent. or more of glucose, the mixture becomes perfectly colorless.

(3) To 0.1 c.c. of the cerebrospinal fluid are added 1.0 c.c. of 0.004 per cent. methylene blue solution and three drops of 10 per cent. potassium hydroxid solution. It is heated and boiled for a few seconds. If the fluid contains 0.1 per cent. or more of glucose, the mixture becomes perfectly colorless.

(4) To 0.5 c.c. of the cerebrospinal fluid are added 1.0 c.c. of 0.004 per cent. methylene blue solution and three drops of 10 per cent. potassium hydroxid solution. It is heated and boiled for a few seconds. If the fluid contains 0.02 per cent. or more of glucose, the mixture becomes perfectly colorless.

THE QUANTITATIVE TEST

After numerous experiments, we found that the quantitative determination of the glucose in the spinal fluid by means of the methylene blue solution is best performed in the following way:

To 1.0 c.c. of 0.004 per cent. methylene blue solution are added three drops of 10 per cent. potassium hydroxid solution. Adding the spinal fluid to be tested from a buret, we determine the minimal volume of it, with which this mixture becomes perfectly colorless by boiling. When the minimal volume (c.c.) is determined, the amount of the glucose present is calculated from the formula: $\frac{0.01}{n} = p$, where p is the percentage of glucose in the cerebrospinal fluid, and n is the number of c.c. of cerebrospinal fluid used. If, for example, the minimal volume of the spinal fluid used is 0.5 c.c., we find the amount of the glucose present as follows: $\frac{0.07}{0.5} = 0.02$ per cent.

SUMMARY

A simple method is described for the determination of glucose in the cerebrospinal fluid. This method is much more convenient than the usual methods and is sufficiently accurate.

Book Review

ORTHOPAEDICS FOR PRACTITIONERS. By P. B. Roth, F.R.C.S. (Eng.). London, Edward Arnold, 1920.

There is much in the book of general interest. The style is good: the reader's interest is held, and the book is a distinct addition to the class of handbooks now being written for the use of practitioners. The author has decided views on the different subjects presented, and does not hesitate to state concisely that which he thinks should be the treatment selected. Such dogmatic statements readily permit of discussion, therefore, the book is open to criticism. However, as the author makes clear in the preface that he is presenting the methods used in his own practice, we can find fault with a type of book which prevents a freer discussion of different methods. There is so much that is sound, that even though one may differ very decidedly regarding some of the lines of treatment laid down, the subject, as a whole, is very well presented.

The American surgeon might well take issue with certain lines of treatment. For example, the author advises tenotomy in torticollis cases and condemns the open method. He condemns the operation of resection of the knee for tuberculosis in adults but one cannot help feel that it is because he delays resection too long. We can, however, agree with him that resection is not best in children. His discussion of fractures is limited, and few men, in America, at least, will agree as to the advisability of using the Lucas-Championnière treatment. No mention is made of the efficient and well established Whitman abduction method for the treatment of fractures of the neck of the femur. In fact, very little is said on this important subject. The presentation of the methods of Hugh Owen Thomas in orthopedic surgery is most valuable for every surgeon, both general and orthopedic, should be familiar with these. Certain details of practice are valuable, such as the treatment of corns, claw foot and hallux valgus. He condemns the operation of excision of the head of the metatarsal, whereas in many hands it has been very useful and certainly does not deserve the sweeping condemnation leveled at it by the author. The chapter on Thomas splints at the last of the book is valuable. On the whole, the book is well worth while, but there has been, perhaps, a little too much disregard for the methods and practices of others.

THE PRINCIPLES OF ANTENATAL AND POSTNATAL CHILD PHYSIOLOGY, PURE AND APPLIED. By W. M. Feldman, M.B., B.S. (Lond.) Assistant Physician to and Lecturer on Child Physiology at the Infants Hospital, with 6 Plates and 129 Illustrations. Longmans, Green & Co., 39 Paternoster Row, London, E.C. 4, Fourth Avenue and Thirtieth Street, New York. Bombay, Calcutta, and Madras, 1920. All Rights Reserved.

The scope of this book is very comprehensive. The introductory outline gives the differences between adult and child and divides the field of child physiology into several periods: (a) *Ante-Natal*: 1. Ante conceptional. 2. Conceptional. 3. Post-Conceptional or intra-uterine. I. Germinal. II. Embryonic. III. Foetal. (b) *Natal* (c) *Post-natal*: I. Neonatal. II. Infancy. III. Childhood. IV. Puberty.

The field the book covers is, perhaps, illustrated best by a citation of the Chapter headings:

Chapter I. Introductory. II. The Germinal Cells (etc.). III. Fertilization or Physiology of Conception. IV. The Nature of Hereditary Processes. V. Mendel's and Galton's Laws of Heredity. VI. Theories of Development. VII. The Mechanics of Development. VIII. The General Physiology of Pre-Natal Development and Metabolism. IX. The Nutrition of the Embryo and Foetus. X. Foetal Respiration. XI. The Pre-Natal Circulation. XII. Foetal Blood. XIII. Foetal Secretions. XIV. Foetal Excretions. XV. The Foetal Muscular System. XVI. The Foetal Nervous System. XVII. The Foetal Sense Organs. XVIII. The Bio-Dynamics of Growth. XIX. The Physiology of Pregnancy. XX. The Physiology of Birth. XXI. The Physiology of the Neo-Natal Period. XXII. The Chemical Basis of the Child's Body (etc.). XXIII. The General Skeletal Anatomy of the Infant Compared with That of the Adult. XXIV. The Physics and Physiology of Bone. XXV. The Muscular System. XXVI. The Mechanics of the Body. XXVII. The Physiology of the Skin in Infancy and Childhood. XXVIII. Respiration. XXIX. The Blood. XXX. The Circulation. XXXI. The Physiology of the Alimentary Tract. XXXII. The Urinary System. XXXIII. The Metabolism of the Child. XXXIV. Dietetics. XXXV. The Nervous System. XXXVI. Vision. XXXVII. Hearing. XXXVIII. The Internal Secretory Glands. XXXIX. Puberty or Adolescence. XL. Post-Natal Growth. XLI. The Physiology of the Premature Infant.

The author states in the preface: "It then occurred to me that, as no attempt had been made to summarize the numerous investigations carried out during the last thirty years, or so, in various parts of the world, in the biology and physiology of child life, from the germinal period onwards, I might be supplying a want if I were to collect, summarize and knit together into a systematical monograph, the information so widely scattered in very many journals and these in various languages." It seems that the author wants to knit together too much in several of the chapters. A number of statements which might be overlooked in a less pretentious volume should be corrected in later editions. For instance, the statement (p. 3) that the loss of heat from the body takes place, for the most part, through the skin by conduction and radiation, should, at least, be modified. The myth that young infants are unable to digest starch easily might be dropped. It might be mentioned that homogentisic acid is classified as amino-acid. It is not easily understood what is meant by "differences in function" in the following sentence: "Indeed, we may define child physiology as the study of the physical and chemical differences in structure, as well as the difference in function, between the various organs of the child's body and those of an adult." More stress might be laid on the differences in the proportion in which the organ systems of the child participate in the body.

To show the importance of the prenatal period, the author indulges in a very painful calculation: From birth to adult age, the child increases only twenty-fold in weight, and about three and one-half times in length; the increment in weight from impregnation to birth is no less than 906 million-fold, and the increase in length is 2,500 fold.

The book is certainly unique. The author thinks it will be found most useful by the physiologist who is occupying himself with the investigation of problems in connection with child life. The pediatric physician is to find it of service as a book of references. This is no doubt the case. As the book is not intended primarily for the pediatrician, it is not necessary to discuss it more extensively. It may be regarded as an interesting and in many ways useful addition to the library.